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EFFICACY OF SOME ANTHELMINTICS

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INTRODUCTION

Although the use of anthelmintic treatment is an old practice in human and veterinary medicine, the efficacy of the various substances employed as anthelmintics is not well known. What information is available is based largely on clinical observations, efficacy being judged to a large extent on a consideration of the improvement or lack of improvement in the patient's health after treatment. In other instances the efficacy of the treatment has been checked by fecal examinations for worms passed and for eggs persisting in the feces; but, while this method gives real and valuable information, it is somewhat inexact. The methods employed for examining feces for worms passed are often rather casual; and negative findings in examining feces for eggs, especially when a small number of preparations are examined for only a few days after treatment, are not always conclusive.

A more satisfactory method of investigating anthelmintic efficacy is to administer treatment to animals, to collect all feces passed for a number of days, to recover from them all worms present, and then to kill the animals and collect all worms remaining. In this way it is possible to arrive at a fair idea of the anthelmintic effect to be expected from a drug, the correctness of the conclusions depending, of course, on the number of experimental animals used and their degree of infestation.

While it is thus possible to express the efficacy of a drug in the form of a mathematical ratio, the writers are fully aware that such ratios, except when based on extensive data, can not be considered an accurate index of the efficacy of the drug, since many factors, not entirely within control, such as the individual reaction of the animal, the amount of material in the alimentary tract, and the potency of the drug, all enter into the problem.

In carrying out this series of experiments the plan of the writers was to test as many drugs as possible having a known or alleged anthelmintic value, abandoning those which gave no results, and making further

[1] Resigned September 19, 1916.

experiments with the more promising. It is therefore possible that some of the drugs tested only once and on a limited number of animals may have more anthelmintic value than the tests indicate. On account of the extent of the field to be covered, the writers did not feel justified in devoting more effort to those drugs which gave small promise of success.

Some such method as the above has been employed by previous investigators. Hutcheon (*1891*)[1] made numerous tests of anthelmintic treatments for stomach worms in sheep and goats in South Africa, and followed the treatments by post-mortem examinations to determine the immediate effect on the worms. Stiles (*1901*, *1902*) did similar work in this country, and a number of veterinarians and stockmen made investigations involving treatment, post-mortem examination, and clinical observation. But, so far as the writers are aware at present, a detailed series of experiments covering the treatment of animals and the collection of all worms from the feces for a number of days up to the time of making a post-mortem examination in which all worms remaining were collected, has not been reported.

In this work the following method was pursued: The animals were given an appropriate dose of the anthelmintic to be tested, the method of dosage varying with the purpose of the experiment and the substance to be tested, preliminary purgation being undertaken or omitted as desired. Treatment was usually administered in the morning, and all feces were collected every morning thereafter until the animal was killed. The feces were washed through a set of graded screens and the screens examined for worms. The animal was usually killed the morning of the fourth day after the administration of the last dose of the anthelmintic, and all parasites remaining were collected and counted.[2] The percentage of efficacy was then estimated from the number of worms found on post-mortem examination and that number plus the number passed after treatment. When preliminary purgation was resorted to, the feces were collected on the following day, the day of administering the anthelmintic, to ascertain what worms if any were removed by simple purgation.

For convenience we have arranged our experimental data in three groups: (1) Simple purgatives, (2) a group including anthelmintic shaving a mineral base and coal-tar products, and (3) a group covering the vegetable anthelmintics. Tables I to V of the discussion of results summarize the results of the experiments.

[1] Bibliographic citations in parentheses refer to "Literature cited," p. 446–447.

[2] In conducting these experiments the writers occasionally found on post-mortem examination dead worms in the large intestine or rectum which normally are found in the small intestine. In such cases, as the worms were evidently in the process of passing out, they are credited as being removed by the anthelmintic.

EXPERIMENTS WITH SIMPLE PURGATIVES

CALOMEL

FOR WORMS IN DOGS.—Calomel in fairly large single doses followed by castor oil proved inefficacious as a remedy for ascarids in dogs. Four infested pups weighing 3.6 to 4.5 kgm. were fasted from noon of the day before treatment, given 4 to 5 gm. of calomel, and on the day following treatment given 15 mils (milliliters) of castor oil. Three of the dogs passed no worms after treatment; one passed a single ascarid (*Belascaris marginata*). Two of the dogs which passed no worms when examined post-mortem showed 10 and 8 *B. marginata*, respectively. The treatment was so evidently inefficacious that the other two dogs were not sacrificed for post-mortem examination. The results of this experiment do not accord with the claims occasionally made as to the anthelmintic value of simple purgatives and cathartics.

CASTOR OIL

FOR WORMS IN DOGS.—Although the efficacy of castor oil as an anthelmintic was not tested as a separate experiment, in several experiments it was given as a preliminary purge. The feces passed following its use were examined, and the worms passed compared with the number found post-mortem. In these experiments only 24 hours were allowed between the administration of the oil and the subsequent anthelmintic. It is therefore possible that the oil alone might have shown greater efficacy if the feces were collected for a longer time. However, in our experience the greater number of worms are passed within 24 hours after the administration of an anthelmintic; and in the case of a drug like castor oil, which usually acts within a few hours after its administration, it is not likely that the conclusions of the writers are much in error.

In 11 experiments in which castor oil was used as a preliminary purge on 50 dogs it removed 27 *B. marginata* out of a total of 351. Its effect on hookworms (*Ancylostoma caninum*) and whipworms (*Trichuris depressiuscula*) was practically nil. It was ineffective more frequently than it was effective, and in no case did it remove all the ascarids from a single dog. It has therefore little to recommend it as an anthelmintic. It may, however, have some diagnostic value in veterinary practice to confirm a clinical diagnosis of ascarid infestation in dogs when a microscopic examination of the feces is impossible, though it is evident that even for this purpose it would not always be reliable.

When worms are passed as the result of the increased peristalsis due to a simple purgative, there is always the suspicion that the worms were dead and would have passed out anyway and that the purge merely hastened their removal.

EPSOM SALT

FOR WORMS IN DOGS.—Epsom salt was tested once as a preliminary purge on three dogs which were given the salt in molasses at the rate of 4 gm. to each 5 kilos of weight. It had no effect on ascarids (*Belascaris marginata*), hookworms (*Ancylostoma caninum*), whipworms (*Trichuris depressiuscula*), *Dipyidium caninum*, or *Taenia pisiformis*, all of which were found present at post-mortem examination. Epsom salt is extremely distasteful to dogs and is likely to promote vomiting. The salt is best given in a vehicle like molasses, which serves to disguise the taste. Aside from this objectionable feature, the salt is less effective in dogs than other purgatives, such as castor oil or calomel, and is not particularly useful in canine practice.

FOR WORMS IN HOGS.—Campbell (*1917*), in a discussion of the treatment of swine for worms, mentions the use by a western veterinarian of Epsom salt dissolved in the drinking water. He says that the hogs are kept away from water for 12 to 24 hours, in warm weather not so long, in cold weather even longer. One ounce (28.35 gm.) of the salt is allowed for pigs and up to eight ounces (226.79 gm.) for hogs, then twice this quantity is added to allow for waste. It is then given in the drinking trough. The pigs being thirsty drink it. This completes the treatment. A test of this treatment was made by the junior writer on two pigs weighing about 23 kgm. (50 pounds) each. The animals were kept in separate pens on board floors and deprived of both food and water for 24 hours. Each pig was then given 226.8 gm. (8 ounces) of Epsom salt dissolved in about 3.8 liters (1 gallon) of water and placed in the drinking troughs. The pigs took a few swallows of the water and refused to taste more, showing their resentment by overturning the troughs and spilling the contents. The experiment was therefore repeated a few days later, the troughs being nailed to the floor. After 24 hours without food or water the pigs were given the salts as before and as in the previous experiment, took only a few swallows, refusing to drink more. Although no other water was given them for the next 24 hours, the troughs remained apparently as full of the salt solution as at the beginning of the experiment. As the pigs had now been without food and had drunk practically no water for 48 hours, the salt water was removed and fresh water and food given. The examination of the feces during the next three days revealed no parasites excepting one nodular worm (*Oesophagostomum dentatum*). The pigs were not killed, as the experiment was evidently a failure. A microscopic examination of the last fecal samples collected showed numerous ascarid eggs.

As it was evident that the Epsom salt in a solution of the strength given was extremely distasteful, it was decided to repeat the experiment with a weaker solution which the pigs might be induced to drink if sufficiently thirsty. Accordingly, the pigs were again deprived of food and

water for 28 hours and then given a solution made by dissolving 0.45 kgm. (1 pound) of Epsom salt in 22.7 liters (6 gallons) of water. As the drinking troughs would hold only 3.8 liters (1 gallon) each, each trough when full contained 75.6 gm. of the salt in solution. It was intended to refill the troughs as fast as they were emptied until each pig had taken 11.35 liters (3 gallons) of the solution, or 226.8 gm. of Epsom salt.

As in the previous experiment, the pigs merely tasted the solution and refused to drink more. No other water was given them for the next 28 hours during which time they had two meals of dry feed. As the pigs had now been without a drink for 56 hours, the experiment was closed. Another microscopic examination of the feces passed at the close of the experiment revealed the presence of ascarids in both pigs.

It is evident from the above that a solution of Epsom salt, even when less than 2 per cent in strength, is so distasteful to pigs that they will not drink it even after a relatively long period of thirst. It may also be noted that 11.4 liters (3 gallons) of water is much more than a pig of 22.67 kgm. (50 pounds) weight could consume in a day even if very thirsty, so that even if the pigs had drunk the weaker solution the treatment would have had to be prolonged for two or three days, greatly decreasing the purgative effect to be expected from a single dose of a large quantity of Epsom salt.

In this connection it may be stated that in an experiment with oil of chenopodium on hogs, conducted some years previously by the junior writer, four hogs were given 113.4 gm. (4 ounces) of Epsom salt mixed with a bran-mash feed, all the animals eating together. No difficulty was experienced in getting the animals to eat the mixture, but the amount of the salt allowed to each hog was only one-eighth of the dose allowed in the present experiment.

EXPERIMENTS WITH ANTHELMINTICS OF A MINERAL NATURE AND COAL-TAR PRODUCTS

TARTAR EMETIC

FOR WORMS IN HOGS.—Tartar emetic is commonly used as a remedy for roundworms in horses, and this led the writers to test its effects upon worms in hogs. Two small pigs were used, weighing 8.6 and 14.5 kgm. They were each given 259 mgm. of tartar emetic dissolved in water, followed after a short interval with 29.57 mils of castor oil. Winslow (*1913*) gives the emetic dose of tartar emetic for hogs as 4 to 10 grains (259 to 648 mgm.). The drug in this case exerted no emetic effect. One of the pigs passed 5 ascarids (*Ascaris suum*) after treatment and showed the presence of 5 others on post-mortem; the other pig passed none and showed 19 on post-mortem. Owing to the more or less common habit which pigs have of devouring ascarids, it is possible that the second pig also passed worms which were eaten; and the first may have passed

more than were recovered in the feces saved after treatment. A few whipworms (*Trichuris suis*) and nodular worms (*Oesophagostomum dentatum*) were passed; a few of the former were found in one of the pigs post-mortem, not looked for in the other, and about 250 and 500 nodular worms were found, respectively, in the two pigs post-mortem.

This experiment demonstrated that tartar emetic has an anthelmintic action on worms in swine, but further trials will be necessary before conclusions can be drawn as to its efficacy. The method of administration used in the experiments is not likely to prove suitable in practice.

CHLOROFORM

Chloroform has been more or less used for some time, either alone or in combination with other substances, as an anthelmintic. Recently Alessandrini (*1915*) has commended it very highly for use against hookworms and other worms. He states that it has these advantages: Combined with castor oil it requires no special preparation of the patient; it can be administered in a single dose; it does not cause local or general disturbances either immediately or subsequently; it is perfectly well tolerated and is not nauseous. It may be given in 3- to 4-gm. doses dissolved in olive oil or castor oil and is thoroughly efficacious against hookworms, whipworms, pinworms, and ascarids. Chloroform is a constituent of Hermann's mixtures, the formula of one of which is given on page 403. Schultz (*1911*) finds the chloroform to be the active anthelmintic ingredient of Hermann's white mixture. He found chloroform very effective against hookworms in the dog and says of it:

> It has proven rapid in its action and thus far not followed by any evil after effects. Should the chloroform-castor oil mixture act as favorably in human beings as it has for me in dogs, it will prove a universal worm remedy of great importance.

In view of the irremediable damage resulting from overdoses of chloroform, Schultz is inclined, however, to favor the use of the less effective drug thymol. Billings and Hickey (*1916*) use a chloroform-castor-oil mixture following the use of chenopodium in the treatment of hookworm and other roundworm parasites of aliens detained at the immigrant station at Angel Island, California. For an adult they administer 20 mils of a mixture of chloroform and castor oil containing 1.8 mils of chloroform. The dose is graduated according to the apparent age.

The writers' experiments with chloroform as a drug for expelling hookworms from dogs inclined them to the belief that it was extremely satisfactory compared with thymol, and on the suggestion of Dr. Charles Wardell Stiles, of the United States Public Health Service, a note was sent to Dr. Reid Hunt, of Harvard University, asking his opinion as to the danger of the administration of chloroform. In his reply he states:

> It has been shown . . . . that even one administration of chloroform causes distinct changes in the liver, from which, however, animals almost always completely recover. I presume that a single dose is efficient and ordinarily harmless; but I think that if the

liver or heart had already been injured or diseased, a single does might have serious consequences. It would seem advisable not to repeat a dose for several days at least.

The experiments of the writers with chloroform were as follows:

FOR WORMS IN DOGS.—Five dogs, weighing from 5.5 to 17.7 kgm., were given, in the morning after fasting from the evening of the day before, 0.2 mil of chloroform per kilo of body weight mixed with 3 mils of castor oil per kilo of body weight. All of the dogs were infested with hookworms (*Ancylostoma caninum*), four very lightly, one heavily, three had a few ascarids (*Belascaris marginata*), four a few (1 to 27) whipworms (*Trichuris depressiuscula*), two a few tapeworms (*Dipylidium caninum*), and one numerous (250) tapeworms of the same species. The dog which had the single hookworm failed to lose the parasite as a result of the treatment, but none were left in the other lightly infested dogs, while more than half the hookworms were passed by the heavily infested dog (457 passed and 355 found post-mortem). One dog passed a single ascarid and showed none post-mortem, two others showed 1 and 2 ascarids, respectively, post-mortem, but had passed none after treatment. Two of the dogs out of the four infested with whipworms passed a few of these worms, and all four showed a few on post-mortem. After the treatment no tapeworms were recovered from the feces of the dogs infested with *D. caninum*.

In this experiment chloroform and castor oil proved rather highly efficacious in removing hookworms, removing all in three cases of light infestation, failed to remove any in one case, and removed over half of the parasites in a case of heavy infestation. The results in the case of ascarids and whipworms are not striking. In the case of *D. caninum* there is no evidence that chloroform is of value as an anthelmintic.

The failure of chloroform to remove all the hookworms from the heavily infested dog indicates that repeated treatments may be necessary in cases of heavy infestations, but in view of the dangers attending the use of chloroform the advisability of repeating the dose is questionable. Several days at least, perhaps a week or longer, should be allowed to elapse to allow time for the animal to recover from the possible ill effects of the first treatment. Further experiments are desirable.

A further test of the efficacy of chloroform in combination with other drugs as an anthelmintic for hookworms in dogs was made with the remedy in the form of Hermann's mixture. This preparation consists, according to Railliet (*1915*), of the following:

Oleoresin of male-fern	4 gm., or
Oil of eucalyptus	2 gm.
Chloroform	3 gm.
Castor oil	40 gm.

He suggests its use as a substitute for thymol. Although the preparation is intended to include either male-fern (*Dryopteris filix-mas*) or eucalyptus oil, through an error both drugs were included. In conducting this experiment two objects were aimed at: (1) To determine whether

or not the chloroform was the sole or principal cause of the efficacy of the mixture as a remedy for hookworms (*Ancylostoma* spp.); (2) whether the combination of castor oil and male-fern was likely to produce symptoms of male-fern intoxication, owing to its greater degree of absorption when combined with an oil.

After a fast of 24 hours, two dogs weighing 9.5 and 16.5 kgm., respectively, were given the full dose of Herman's mixture as detailed above. Two other dogs weighing 9.6 and 12.4 kgm., respectively, were given the mixture without chloroform. Nearly three-fourths of the hookworms (*Ancylostoma caninum*) in the two dogs receiving the full mixture were eliminated by the treatment, one dog passing 16 *A. caninum* after the treatment and having only 3 left at the post-mortem examination. On the other hand, out of 39 *A. caninum* in the two dogs receiving the mixture without chloroform, only 3 were eliminated. The mixture without chloroform showed some slight efficacy for whipworms, but the figures are not striking. Two of the dogs were infested with *Dipylidium caninum*, one passing a number of fragments with several heads within 30 minutes after dosing. The other dog passed a few segments. Both dogs were found free from *D. caninum* at post-mortem examination. As these dogs had received the mixture without chloroform, it is evident that the tæniacidal value of the mixture was due to the male fern or eucalyptol and not to chloroform. This may reasonably be considered a demonstration of the efficacy of male fern as a tæniacide.

To sum up, it appears from the above that Hermann's mixture (including both eucalyptol and male-fern) is an efficient vermifuge for hook worms, owing largely, if not entirely, to the chloroform content. It is also efficacious for *Dipylidium caninum*, probably on account of the male fern it contains. It seemed to have some slight effect on whipworms, but the evidence of this was by no means convincing. The combination of male-fern and castor oil seemed to have no deleterious effect on the experiment animals, in this respect supporting the opinion of Lenhartz (*1902*) and Seifert (*1908*). Further experimentation, however, is desirable to elucidate this point.

FOR WORMS IN SHEEP.—Chloroform was tested on two sheep weighing 25 and 28 kgm., respectively. The dose for each was mixed with 60 mils of castor oil, the smaller sheep receiving 5 mils of chloroform (0.2 mil per kilo) and the other 10 mils (nearly 0.4 mil per kilo). Both sheep died four days after dosing and showed, on post-mortem examination, lesions of gastro enteritis and pneumonia in the congestive stage. The sheep were very lightly infested with parasites. None were recovered from the feces of the sheep which received the smaller dose; three stomach worms (*Haemonchus contortus*), five nodular worms (*Oesophagostomum columbianum*), and five hookworms (*Bunostomum trigonocephalum*) were found in this sheep post-mortem. The sheep which received the larger dose passed nine stomach worms and one nodular worm after treatment, and two stomach worms were found post-mortem.

The chloroform had an evident anthelmintic effect on the sheep which received the larger dose. The fatal results of the treatment in both cases, however, indicate that chloroform is not a promising anthelmintic for use on sheep.

ETHER

FOR WORMS IN DOGS.—Four dogs weighing from 2.38 to 4.89 kgm. were given ether in a dose of 0.8 mil per kilo mixed with 15 mils of castor oil for the two smaller dogs and 30 mils of castor oil for the two larger dogs. The afternoon of the day before treatment the dogs were given a preliminary dose of castor oil, and were not fed until several hours after receiving the ether. No worms were recovered from the feces passed between the administration of the preliminary dose of castor oil and the administration of the ether and oil mixture. This mixture was much resented by the dogs, and all of them were salivated by it and showed more or less evidence of collapse. One of the dogs passed a few tapeworm segments (*Taenia pisiformis*), but no other tapeworm material was recovered from the feces; nor were any tapeworms found post-mortem. No hookworms were recovered from the feces, but all showed infestation on post-mortem examination, the number of worms being 7, 21, 233, and 242, respectively. One of the dogs passed 1 ascarid and one passed 6. At the post-mortem examination no ascarids were found in the former and 11 in the latter. The other two passed no ascarids; 4 were found post-mortem in one, but 1 of these was in the rectum, evidently about to be passed; 1 ascarid was found post-mortem in the other of these two dogs.

The conclusion from this experiment is that the ether exhibited a rather slight anthelmintic action against ascarids, no evident action against hookworms, and probably was instrumental in the removal of a tapeworm which was presumably present in one of the dogs, in view of the discovery of segments in the feces.

IODOFORM

FOR WORMS IN DOGS.—Among the remedies prescribed for ascarids in human subjects iodoform has been occasionally recommended. Schidlowski (*quoted by Seifert, 1885, p. 98*) gives it in the form of a powder mixed with sodium bicarbonate in doses of 0.01 to 0.06 gm. three times a day, followed by a dose of castor oil on the last day. In the present experiment it was intended to give the maximum amount, 0.18 gm., in one dose to each of four dogs ranging in weight from 11.8 to 14 kgm. However, through an error in weighing the drug, the dogs were each given 0.018 gm. instead of 0.18 gm. This error was discovered afterward, and the next day the full dose, 0.18 gm., was given. Thus, each dog received a total of about 0.2 gm. of iodoform, given in capsule with sodium bicarbonate. The dogs were starved for 24 hours before treatment, and allowed one meal between the first and second doses. After each dose 29.6 mils of castor oil were administered. One Taenia segment was passed by one

of the dogs, no worms being recovered. As the treatment was obviously inefficacious, only two of the dogs were killed. The post-mortem examination showed these animals infested with various numbers of intestinal nematodes and tapeworms. As far as can be judged from a single experiment, iodoform is valueless as an anthelmintic for intestinal parasites in dogs, even when given in doses in excess of that prescribed for human subjects.

COPPER SULPHATE

FOR WORMS IN SHEEP.—The use of copper sulphate as an anthelmintic against stomach worms in lambs was developed by Hutcheon (*1892, 1895*), who reported thousands of cases of its successful use in South Africa. His favorable reports were based largely on clinical findings, but in a number of cases he treated animals with the copper-sulphate solution and killed them a short time afterward to determine whether the worms in the stomach were dead or alive. The solution he used is approximately that which would be obtained from 0.45 kgm. of pure copper sulphate, powdered fine and dissolved in 35.96 liters of warm water. Only clear blue crystals are used, and it is best to powder these and then to dissolve the powder in a small quantity of hot water and to add cold water to make up the required amount. He gave the solution in the following doses.

Lambs 3 months old	¾ ounce (22. 17 mils).
Lambs 6 months old	1½ ounces (44. 56 mils).
Sheep 12 months old	2½ ounces (73. 9 mils).
Sheep 18 months old	3 ounces (88. 7 mils).
Sheep 24 months old	3½ ounces (103. 5 mils).

Stiles and others have tested and recommended copper sulphate in these doses.

It did not appear to the writers that such refinement in dosing was called for in treating sheep; therefore, for the sake of simplicity a 1 per cent solution was made up and administered in amounts of 100 mils to sheep a year old or older, and in amounts of 50 mils to lambs under a year old.

Five sheep less than a year old were dosed with copper sulphate, two receiving 0.5 gm. each of powdered copper sulphate in capsule, and three receiving 50 mils each of the 1 per cent solution.

The two sheep receiving powdered copper sulphate in a capsule passed a few stomach worms, and on post-mortem showed over 6,000 in one case and over 4,000 in the other. No nodular worms were recovered from the feces, but the post-mortem examination showed over 100 in one case and nearly 200 in the other. Both showed a few tapeworms (*Monezia* sp.) and hookworms post-mortem, none having been recovered from the feces after treatment. Several other species of nematodes were also found in varying numbers at the post-mortem examination.

The three sheep which received the copper-sulphate solution passed, respectively, 120, 240, and 314 stomach worms, and showed on post-

mortem 0, 49, and 3, respectively. There was no marked effect upon the nodular worms, although one of the sheep passed 2 worms of this species, 175 were found post-mortem, and 143 and 21, respectively, were found in the two others, from whose feces none were recovered after treatment. Two of the sheep showed hookworms on post-mortem examination, and, although none were found in the other one, it is quite probable that none were present when the animal was treated, as none were recovered from the feces after treatment.

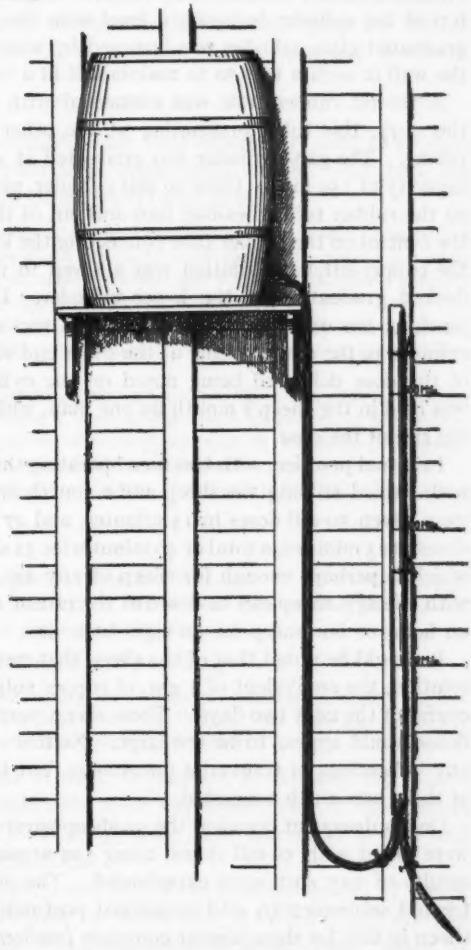

FIG. 1.—Apparatus, with control, for administering copper-sulphate solution to sheep.

Evidently the powdered copper sulphate in capsule exhibited no anthelmintic action. On the other hand, supporting the experience of Hutcheon, Stiles, and others, a 1 per cent copper-sulphate solution in 50-mil doses proved very efficacious in the removal of stomach worms. It had no evident effect upon other intestinal parasites.

In view of the efficacy of the copper-sulphate solution, a test was made to determine how readily and easily it could be administered, with a view to determining whether large numbers of animals could readily be treated with the solution. A dosing apparatus devised by the senior writer was constructed and used as follows:

A 1 per cent solution of copper sulphate was made up and placed in a small water-tight keg (fig. 1). At the side of the keg, near the bottom,

a perforated cork with a glass tube through the perforation, was inserted in an auger hole. A rubber tube was connected with the glass tube. The keg was placed on a high shelf in the barn and the rubber tube from the bottom of the keg connected with one of two glass tubes that perforated a rubber cork in the bottom of a graduated glass cylinder, the top of the cylinder being on a level with the bottom of the keg. The graduated glass cylinder was fastened by wires to two nails driven into the wall in such a way as to maintain it in a vertical position.

A second rubber tube was connected with the second glass tube in this cork, this tube terminating at the other end in a piece of metal tubing. The glass cylinder was graduated at 50-mil intervals and had a capacity of 150 mils. Close to this cylinder, pinch controls were fastened on the rubber tubing leading into and out of the cylinder. By pinching the control on the rubber tube connecting the keg with the glass cylinder, the copper-sulphate solution was allowed to flow from the keg to any desired graduation in the lower cylinder. By letting this close and pinching the other control, the solution was allowed to flow from the cylinder to the metal tubing at the other end of the dosing tube, the size of the dose delivered being noted on the cylinder. The metal tubing was held in the sheep's mouth by one man, while another man controlled the size of the dose.

In actual practice, with two men operating this apparatus, as noted, and with a third holding the sheep and a fourth bringing them up, 25 sheep were given 50-mil doses in 15 minutes, and 27 sheep were given 100-mil doses in 25 minutes, a total of 40 minutes for 52 sheep. In the 50-mil dose, which is perhaps enough for sheep of any age, since it combines safety with efficacy, sheep can be dosed at the rate of 1⅔ a minute. This is 100 an hour, or 800 sheep for an eight-hour day.

It should be noted that of the sheep that received 100-mil doses of the solution, the equivalent of 1 gm. of copper sulphate, 2 sheep died in the course of the next two days. These sheep were 10 months old, and these doses would appear to be too large. Neither of the dead sheep showed any indications of traumatic pneumonia, but the fourth stomach of one of them was much congested.

On a subsequent occasion the 50 sheep surviving from this experiment were dosed with 50-mil doses, using the apparatus described. No bad results of any sort were experienced. The sheep have been similarly treated subsequently, and occasional post-mortem examinations of the sheep in this lot show almost complete freedom from stomach worms.

COPPER SULPHATE

FOR WORMS IN DOGS.—In view of the efficacy of copper sulphate against stomach worms in sheep, an attempt was made to determine whether the well-known emetic action of this drug would entirely prevent its use as an anthelmintic for dogs. Four dogs were each given 0.5 gm. of copper

sulphate dissolved in 10, 20, 30, and 40 mils, respectively, of water, and 2½ hours later they were given 14.79 to 29.57 mils of castor oil each. There was prompt emesis in a few minutes after the administration of the copper sulphate. Fecal examinations for the following four days showed only 1 worm, a whipworm. Because of the evident defects of the treatment, the dogs were not killed and examined. It is obvious that the emetic action of copper sulphate precludes the use of this substance as an anthelmintic for dogs.

GASOLINE

FOR WORMS IN SHEEP.—Gasoline has been extensively used as a treatment for stomach worms, but some authorities consider that there are dangers attending its use. Stiles (*1901*) says of it:

> Gasoline has recently gained considerable reputation as a vermifuge. I have used it in a number of cases and have found the claims made for it to be more or less justified. Three objections, however, arise to its use, and I can not, therefore, consider it an ideal treatment. These objections are:
>
> (1) Not less than three doses, and usually four to six, are required to expel the worms.. Its use involves a great expenditure of labor, and it is, therefore, impracticable on the large ranches.
>
> (2) While several doses are not necessarily injurious to the stock, still, if the doses are large, repeated drenches cause a more or less severe congestion of the bowels. Not only that, but repeated handling of range sheep, with the necessary preliminary treatment of withholding food, is injurious to the animals.
>
> (3) If used on animals suffering from pleurisy, it is likely to be fatal. I have had several fatal cases of this kind.

Luckey (*1915*) says:

> Gasoline for acute cases is a specific. One dose is enough. * * * The average man can not give gasoline without killing the animal. One can not give a sheep with a little bit of pneumonia gasoline without killing it.

Arbuckle (*1916*) says of himself and Joe Wing:

> We were the first men in the country to employ the gasoline treatment successfully. Wing had heard of it as a remedy used in France. We were also among the first to discover that this was not a practicable treatment.

Gasoline is usually given in milk, linseed oil, or flaxseed tea, which makes the treatment considerably more expensive, and, as these feeds are not always available in large quantity, the treatment is not well adapted to the needs of large flocks.

Stiles (*1901*), Ransom (*1907*), and others have recommended ¼ ounce (7.39 mils) of gasoline as the dose for lambs and ½ ounce (14.79 mils) as the dose for sheep. Coffey (*1915*) recommends larger doses; lambs at weaning to get ¼ ounce, ½ ounce, and ¾ ounce, respectively, on each of three successive days; sheep to receive ½ ounce, ¾ ounce, and 1 ounce, respectively, on each of three successive days, these doses to be given thoroughly emulsified in 5 ounces (147.87 mils) of milk linseed oil, or flaxseed tea.

In the writers' first experiment four lambs were treated. Two of them weighing 21.09 and 21.77 kgm., respectively, were given 7.39 mils of gasoline in 148 mils of milk at each dose, the equivalent of the dose commonly recommended, and the others, weighing 26.3 and 22.2 kgm., respectively, were given 14.8 mils of gasoline in 148 mils of milk at each dose, the equivalent of Coffey's doses of ¼, ½, and ¾ ounce for lambs. The dose named was given to the lambs on each of three successive days.

The two lambs which received 7.39 mils of gasoline passed about one-fourth of the total number of stomach worms (*Haemonchus contortus*) present, no hookworms (*Bunostomum trigonocephalum*), of which only a very few were present, and several nodular worms (*Oesophagostomum columbianum*), of which a considerable number were found post-mortem. There was no evident effect on various other species of nematodes and tapeworms present in one or both of the lambs. The two lambs which received 14.8-mil doses of gasoline were more lightly infested; one which passed 58 *H. contortus* showed none on post-mortem; the other passed 4 and showed 2 post-mortem. There was very little effect on hookworms present in small numbers in one of the lambs.

All four of the lambs showed lesions of pneumonia which were suspected to be of traumatic origin.

In the second experiment three sheep were treated. The larger dose of gasoline, recommended by Coffey and found most efficacious by the writers, was employed and was given on each of three successive days by a stomach tube passed down the esophagus, but not far enough to direct the fluid into the rumen. In this way the writers expected to avoid the possibility of causing traumatic pneumonia. None of the sheep passed any stomach worms, and none were found post-mortem, so the experiment throws no light on this subject. The treatment showed a slight efficacy for hookworms (*Bunostomum trigonocephalum*). It failed to remove any nodular worms (*Oesophagostomum columbianum*) from one sheep, but removed all specimens of this species from another lightly infested sheep. It apparently removed all specimens of *Cooperia* sp. from the only animal infested with this parasite.

From this experiment it would appear that gasoline has some slight effect on intestinal worms in lightly-infested sheep, but the evidence is not sufficient to justify its use for this purpose without further experimentation. No lesions of pneumonia were observed in this experiment, although the stomachs of all three sheep showed lesions suggesting healing ulcers with traces of hemorrhage.

As the question of the efficacy of gasoline as a vermifuge for stomach worms in sheep and the likelihood of this treatment's causing lesions of pneumonia and gastritis did not seem to be settled, a further trial of gasoline was carried out by the junior writer. In this experiment two

sheep were used and treated by drenching with increasing doses of gasoline in milk as recommended by Coffey (*1915*). The dosage given was 15, 22, and 30 mils in 236.6 mils of milk on the first, second, and third days, respectively. The same dose was given to each animal.

The first sheep passed no stomach worms and had none on postmortem examination, so the efficacy of the treatment in this case is undetermined. A few hookworms only were passed. The second sheep, which was lightly infested with stomach worms, passed none, but passed a few specimens of hookworms and nodular worms, forming a small percentage of the total number present.

In this experiment, although the sheep received much larger doses than in the previous experiments and the medicine was given in a drench, there were no evidences of pneumonia or gastritis.

Considering the three experiments with gasoline as a whole, involving the use of nine experiment animals, the writers find that this treatment removed over one-fourth of the stomach worms present and had some slight efficacy for hookworms and nodular worms. This compares very unfavorably with the efficacy of copper sulphate for stomach worms when given in solution. The gasoline treatment has also the further disadvantages that it must be given three times, and in a vehicle such as linseed tea or milk, which is an additional expense. There is also the possibility of causing traumatic pneumonia, although the subsequent experiments with this drug indicate that gasoline is not necessarily more dangerous as a drench than is copper sulphate.

PETROLEUM BENZIN

FOR WORMS IN SHEEP.—As already stated, Stiles (*1901*) was favorably impressed with the use of gasoline as a vermifuge in spite of certain objections that he notes. It was suggested by Dr. B. H. Ransom, Chief of the Zoological Division, Bureau of Animal Industry, that our failure to get more satisfactory results might be due to the difference in the commercial gasoline of the present day and that used by Stiles. It was recalled that in 1901, when Stiles conducted his experiments, the automobile industry in this country was in its infancy, and there was little demand for gasoline. Consequently the petroleum distillers included only the most volatile hydrocarbons in gasoline, reserving the heavier fluids for kerosene, their principal product. At the present day, with conditions reversed, the distillation temperatures of gasoline have been greatly extended, with a consequent increase in the specific gravity and lessening of volatility.

In order to determine whether the lessened volatility of the present-day gasoline was related to its inefficacy as a vermifuge, a test was made by the junior writer of petroleum benzin, U. S. P. This product, distilled between 45° and 60° C., represents only the most volatile hydro-

carbons of petroleum and is probably more like the commercial gasoline used by Stiles (*1901*) than the present-day commercial product.[1]

Two full-grown sheep were used for the experiment. The animals were starved for 24 hours and then given 15 mils of petroleum benzin in 150 mils of milk, on three consecutive days. They were drenched through a tube held in the mouth. In no case were any symptons of intoxication from the fumes of the benzin observed during or after its administration, and the post-mortem showed no lesions which could be attributed to the action of the drug.

The chief points of interest in this experiment are:

(1) The apparent superiority of refined gasoline (petroleum benzin) over commercial gasoline as an anthelmintic for stomach worms (*Haemonchus contortus*) and hookworms (*Bunostomum trigonocephalum*). It proved 88 per cent efficacious for stomach worms while the latter was only 35 per cent efficacious, as shown by the summary of three experiments. Its efficacy against hookworms is still more marked. It was 73 per cent efficacious for this parasite, while gasoline proved only 5 per cent efficacious.

(2) Its entire inefficacy against nodular worms (*Oesophagostomum columbianum*). No worms of this species were removed by petroleum benzin, while the three experiments with gasoline showed an efficacy of 16 per cent for this parasite.

The post-mortem examination of the two sheep showed that they were both very lightly infested with stomach worms (*Haemonchus contortus*), most of which had been removed by the treatment. The remedy removed all hookworms (*Bunostomum trigonocephalum*) from one sheep and more than half the number present from the second sheep. It was entirely inefficacious against other intestinal nematodes and tapeworms (*Moniezia* spp.). Its failure to destroy any of the nodular worms (*Oesophagostomum columbianum*) in the large intestine may be explained on the grounds that it is perhaps more readily absorbed than commercial gasoline, and, hence, was largely absorbed before reaching the colon. It should be pointed out that in this experiment the animals were starved for 24 hours before treatment, while in the experiments with gasoline they were not starved. This may have had something to do with the results notwithstanding the slowness with which the rumen becomes empty when sheep are starved.

In summary it may be stated that petroleum benzin showed marked superiority over commercial gasoline as an anthelmintic both for stomach worms (*H. contortus*) and hookworms (*B. trigonocephalum*). While it did not quite equal the treatment with the copper-sulphate drench as a

[1] According to the issue of the Journal of the American Medical Association for October 14, 1916, the present commercial gasoline includes hydrocarbons distilling at a temperature as high as 175° C. (TYDEMAN, F. W. L. NAPHTHALENE IN GASOLINE FOR AUTOMOBILES. *In* Jour. Amer. Med. Assoc., v. 67, no. 16, p. 1175.)

remedy for stomach worms, it was far superior to anything else tried as a remedy for hookworms (*B. trigonocephalum*) and is worthy of further experimentation to test its efficacy on more heavily infested animals. For the treatment of stomach worms copper sulphate must still be considered superior, not only because it is somewhat more efficacious but on account of its lesser cost and the fact that only one dose of copper sulphate is required, whereas three doses of petroleum benzin are advisable.

PHENOLS

The phenols a re a group of organic compounds composed of hydroxy derivatives of the benzene series, the hydroxyl radical being linked directly to the nucleus. The refined phenols include phenol (C_6H_5OH), commonly called carbolic acid; cresol ($C_6H_4CH_3OH$), commonly called cresylic acid or kresol; and the higher phenols. The term "crude phenols" is used in general to designate those unrefined mixtures of the phenols proper with certain hydrocarbon oils and other impurities with which they become associated in the course of their preparation, whether from coal-tar, wood-tar, or blast-furnace gases. There are on the market numbers of trade preparations in the form of soaps, powders, ointments, or liquids which contain refined or crude phenols as essential constituents. A number of these liquid phenol preparations have been used and recommended as anthelmintics. Some of these liquids are insoluble in water, in which case they may or may not be capable of being emulsified, and others are soluble in water.

FOR WORMS IN SHEEP.—Three preparations were tested, which may be referred to as A, B, and C. A and C are advertised as remedies for stomach worms, while B, though not advertised on the container for the treatment of stomach worms (*Haemonchus contortus*), has since been recommended by the New Zealand Department of Agriculture for that purpose. Two sheep were treated with A and one sheep each with B and C. One of the sheep treated with A passed four nodular worms (*Oesophagostomum columbianum*). This sheep and the one treated with B died the day after treatment. The other sheep passed no worms.

Of the two sheep receiving A, the one which died had 422 stomach worms (*Haemonchntortus*) *us co*and numerous intestinal nematodes. The other sheep killed four days after drenching had no stomach worms post-mortem and few intestinal nematodes. As this sheep was evidently uninfested with stomach worms (*H. contortus*), it must be left out of consideration. The sheep treated with C passed no worms and had 8 stomach worms (*H. contortus*) post-mortem.

A second trial was made of A on two sheep, the dose given being the same as in the previous experiment—1 tablespoonful of the product (14.8 mils) to 1 pint (473 mils) of milk, as advertised on the label. The sheep passed no worms, and at post-mortem examination were found lightly infested with stomach worms and intestinal nematodes.

While the experiment is inconclusive in regard to the efficacy of coal-tar phenols for stomach worms in sheep, since the experiment animals were so lightly infested, it failed completely as a remedy for lightly infested animals, and there seems to be no reason for considering that it would be more successful in heavily infested sheep.

There can be little doubt that the treatment is dangerous. Two out of four sheep in the first experiment died, the post-mortem showing lesions of pneumonia, pleurisy, and gastritis. In the second experiment both sheep collapsed after drenching, but seemed to recover. The pneumonic condition observed in the dead sheep may be attributed to getting some of the fluid in the lungs, an error in drenching, to be sure, but one almost impossible to avoid when giving as much as 473 mils of drench. In the writers' experience sheep will usually take quietly 118 to 177 mils of fluid by drench; but, after more is given, they begin to struggle, making the drenching increasingly difficult. Furthermore, the hemorrhagic lesions in the stomach of one of the dead sheep would seem to indicate the absorption of phenols through the gastric mucosa.

FOR WORMS IN DOGS.—A further test of the anthelmintic efficacy of phenols was made, using another preparation, which is recommended as an anthelmintic for worms in dogs, the dose recommended being 5 to 8 drops (0.3 to 0.48 mil) in a tablespoonful (14.79 mils) of castor oil. The writers used 0.48-mil doses, administering this dose to each of two dogs, weighing, respectively, 8.6 and 11.3 kgm. On the fourth day after treatment one dog passed two ascarids and the other passed a headless chain of segments of *Taenia hydatigena*. This latter dog showed an infestation with ascarids (*Belascaris marginata*), hookworms (*Ancylostoma caninum*), and tapeworms (*Taenia* sp.), and, as the treatment had been unsuccessful except for the partial removal of a tapeworm, the animal was not killed. The other dog was killed and found to have three *B. marginata* and three *A. caninum*. The treatment, therefore, was somewhat efficacious against ascarids in one case, but entirely inefficacious in the other. It was effective against *A. caninum* in both dogs. It also appears to be ineffective against Taenia, since it did not bring away the head, but this is a point that should have been confirmed post-mortem.

We may conclude from the experiments on dogs and sheep, above recorded, that the phenols in the form of commercial disinfectants and dips are likely to be of little value and dangerous as anthelmintics.

EXPERIMENTS WITH VEGETABLE ANTHELMINTICS

OLEORESIN ASPIDII

FOR WORMS IN DOGS.—*Oleoresin aspidii* is the classic remedy for use against tapeworm. In the discussion of chloroform as an anthelmintic for hookworms (page 403) the writers have already

shown that male-fern in a combination known as Hermann's mixture is efficacious against *Dipylidium caninum* and may have some slight value against whipworms (*Trichuris depressiuscula*) and hookworms (*Ancylostoma caninum*), although the efficacy of the mixture for hookworms is largely due to the chloroform contained in it. The following experiments in which male-fern alone was used corroborate these conclusions.

In the first experimental test of the drug five dogs were used ranging in weight from 6.4 to 15.9 kilos. The treatment was preceded by calomel (65 to 194 mgm., according to the weight of the animals) the afternoon of the preceding day and followed about 45 minutes after treatment by Epsom salt in molasses. One to three mils of male-fern were administered. Within an hour after treatment one dog had passed a mass of fragments of *Dipylidium caninum*, including at least four heads, and another some chains of segments of *Taenia* sp. When the dogs were killed, no specimens of *Taenia* sp. were found, and only two specimens of *D. caninum*, one of which was in the colon, evidently about to pass out. It is evident that the remedy was entirely efficacious against *Taenia* sp., since the dog which was observed to pass Taenia segments after dosing with male-fern was found uninfested on post-mortem examination. It was slightly less efficacious for *D. caninum*, but apparently removed all but one specimen. It is possible that the male-fern removed all individuals of *D. caninum* not attached by burrowing into the intestinal mucosa, leaving embedded heads to renew strobila. This would account for the failure to find more than four heads in the relatively large mass of segments passed.

Male-fern had but little effect on ascarids (*Belascaris marginata*) and removed only one-fourth of the hookworms (*Ancylostoma caninum*) present, in spite of the fact that at one time it was regarded as an appropriate remedy for hookworms (*A. duodenale*) in man and much used for the purpose. It should be stated, however, that, in view of the small number of hookworms involved in this experiment, only four being present, the conclusion that male-fern is inefficacious against hookworms is hardly warranted. None of the three whipworms (*Trichuris depressiuscula*) present were removed by this drug, although Miller (*1904*) reported the successful removal of whipworms from dogs with it.

A further test of the efficacy of oleoresin of aspidium against tapeworms in dogs was conducted by the junior writer. After the usual 24-hour fast, two dogs weighing 20.4 and 11.34 kgm. were given 2.7 and 1.8 mils, respectively, of male-fern, followed by 162 mgm. of calomel.

Prior to treatment the smaller dog had been repeatedly seen to pass chains of proglottides identified as *Taenia pisiformis*, while only a few Taenia eggs had been seen in the feces of the larger dog. The presence of these eggs may have resulted from contamination of the specimen.

Following the anthelmintic the smaller dog passed a few chains of proglottides the first day after treatment, and on the second day 17 fragments and 4 heads. No tapeworms were passed by the larger dog during the four days following treatment, and no nematodes were passed by either dog. The feces of the larger dog were examined for Taenia eggs four days after administering the vermifuge, and were found negative. As this dog had passed no Taenia, and as the original presence of tapeworms was somewhat doubtful, it was dropped from the experiment. The post-mortem examination of the smaller dog showed no Taenia, 15 hookworms, and 13 whipworms. The remedy was therefore entirely efficacious for species of Taenia and entirely inefficacious for hookworms (*Ancylostoma caninum*) and whipworms (*Trichuris depressiuscula*), thus confirming the opinion derived from the previous experiment, that male-fern is very efficacious for tapeworms in dogs and inefficacious for nematodes.

For worms in cats.—Six cats which had been fed with *Cysticercus fasciolaris* formed the subject of this experiment. Each cat was given 0.8 mil of oleoresin of aspidium, followed by 130 mgm. of calomel for the four largest cats and 97 mgm. of calomel in the case of the two smaller cats. Within half an hour one of the cats, which was weak from confinement in a cage and which was suffering from coryza, had died. The post-mortem examination revealed an intense congestion of the gastric mucosa. The characteristic odor of male-fern was noticeable in the stomach, but not in the intestines. A half-grown individual of *Taenia taeniaeformis* and several ascarids (*Belascaris cati*) were found in the small intestine, while three dead *B. cati* were in the colon. Another cat, which was weak from a previous infestation with mange, passed several chains of *T. taeniaeformis* shortly after the administration of the male-fern and died three days later. A third cat vomited one *T. taeniaeformis* and one *B. cati* and still had one *B. cati* post-mortem. Two of the six cats were uninfested with *Taenia* spp., since they passed no tapeworms and none were found post-mortem. Of the four infested animals two died from the treatment, but three of the four were entirely freed from their Taenia infestation, the fourth dying before the remedy had an opportunity to reach the parasite.

It would appear from the above that male-fern is efficacious in removing tapeworms from cats, but that it is apparently more toxic in the case of cats than with dogs, and should only be prescribed for healthy animals. Probably some other taeniacide could be used which might prove as effective and less dangerous. It should be noted that the dose of male-fern given was less than the minimum dose 15 minims (0.9 mil), recommended by Winslow (*1913*). With the exception of the one ascarid, which was vomited, the treatment had no effect on the few ascarids (*Belascaris cati*) and hookworms (*Ancylostoma caninum*) which were present.

PELLETIERINE TANNATE

FOR WORMS IN CATS.—Pelletierine tannate has long been recognized as an effective taeniacide. According to the U. S. Dispensatory —[1]

The efficacy of pelletierine as a taeniacide has been abundantly confirmed, and it appears to be established that the tannate is the most effective and the least dangerous form of the remedy,—probably because its insolubility prevents its rapid absorption and enables it to come in prolonged contact with the worm.

A test of this drug was made by the junior writer on two cats weighing approximately 3 and 4 kilos each. Sixty-five mgm. of pelletierine tannate per kilo were administered in capsules to each animal and were followed one hour later by 25 mils of castor oil. Prior to the administration of the anthelmintic the cats were starved for 24 hours.

The animals were fed shortly after the administration of the castor oil.

All feces passed during the four days following the administration of the drug were negative for parasites. Cat 2 vomited immediately after feeding, or a little more than an hour after taking the pelletierine. On post-mortem examination cat 1 had 29 *Belascaris cati* and 4 *Dipylidium caninum;* cat 2 had 1 *Taenia taeniaeformis*.

In this experiment pelletierine tannate proved unsuccessful as an anthelmintic for species of Taenia, Dipylidium, or ascarids in cats. The complete failure of the drug is not easy to understand. In the case of cat 2 the drug might have been expelled in the vomitus before it had acted on the Taenia, but this is unlikely, since the vomiting did not occur until more than an hour after the ingestion of the pelletierine.

As the pelletierine tannate used had been in the laboratory for at least six years it was submitted for examination to the Biochemic Division of the Bureau of Animal Industry. The report was returned that the sample responded to all the tests for pelletierine tannate given in the Pharmacopeia. The Pharmacopeia specifies that the drug shall be kept in small well-stoppered bottles away from the light, a condition complied with in this case. There seems to be no reason to suppose that the pelletierine tannate that was used had undergone deterioration, and its failure to give results remains unexplained.

FOR WORMS IN DOGS.—As pelletierine tannate had shown a surprising inefficacy in regard to tapeworms in cats, a further test of this drug was made by the junior writer, using dogs as experiment animals.

The drug was administered to three dogs weighing from 11.8 to 14 kilos, at the rate of 16 mgm. per kilo and was followed one hour later by castor oil. Previous to the treatment 35 mils of castor oil were given to each dog as a preliminary purgative, and the animals were then fasted for 24 hours.

[1] WOOD, G. B., and BACHE, Franklin. THE DISPENSATORY OF THE UNITED STATES OF AMERICA. ed. 19. p. 600. Philadelphia and London, 1907.

Following the administration of the preliminary purgative, two dogs each passed two Taenia proglottides. Following the dose of pelletierine tannate and castor oil, one dog passed five Taenia proglottides, and another dog passed two proglottides. No tapeworm heads or nematodes were found in the feces. The post-mortem examination revealed a few nematodes and *Dipylidium caninum*, but no *Taenia* sp.

It is evident that all three dogs were infested with species of Taenia, since proglottides were recovered in the feces of all animals. The fact that all dogs were free from Taenia on post-mortem examination is indicative of the efficacy of the drug as a taeniacide. The failure to recover the worms in the feces probably resulted from neglect on the part of the attendant collecting the feces.

Pelletierine tannate apparently proved entirely inefficacious against *Dipylidium caninum* or intestinal nematodes in dogs, since none of these parasites was found in the feces, but some were present post-mortem. As there is a strong probability that all feces were not collected, the writers can not be certain with regard to the total inefficacy of the drug for these parasites.

The sample of pelletierine tannate used in this experiment was purchased from the same manufacturer and at the same time as the sample used in the previous experiment on cats. It may therefore be assumed to have the same potency as the sample used in the previous experiment, which was tested for purity by the Biochemic Division.

ARECA NUT

FOR WORMS IN DOGS.—Areca nut (*Areca catechu*) is not infrequently prescribed as an anthelmintic for ascarids in dogs. Railliet (*1915*) gives the dose of areca nut as 2 to 4 gm. combined with 10 to 20 gm. of soluble cream of tartar,[1] the latter presumably being used merely as a vehicle. In this experiment 6 gm. of areca nut and 36 gm. of soluble cream of tartar were formed into 12 pills, 4 of which were given to each of three puppies weighing between 1.8 and 2.3 kgm. Previous to the experiment the dogs were each given 14.79 mils of castor oil, which failed to remove any worms, and were then starved for 24 hours. All the dogs were infested with ascarids (*Belascaris marginata*) and hookworms (*Ancylostoma caninum*), as shown by previous fecal examinations. The day following the administration of the vermifuge one of the dogs passed 4 *B. marginata* and was found dead the following morning. The other dogs passed no worms. The post-mortem of the dog that died showed hemorrhagic areas in the colon and feces stained with blood. The other organs were

[1] Soluble cream of tartar, a preparation seldom used by American veterinarians, is boro-tartrate of potassium, made by boiling together four parts of cream of tartar with one part of boric acid in a large amount of water. When most of the water has evaporated, the process of evaporation is completed in a drying oven and the resultant salt is pulverized and stored in well-stoppered bottles. Soluble cream of tartar is very deliquescent, and hence well adapted for making a pill mass.

entirely normal in appearance. This puppy had 23 ascarids (*B. marginata*) and a few hookworms (*A. caninum*) and whipworms (*Trichuris depressiuscula*). The other dogs had varying numbers of ascarids, hookworms, and whipworms. The treatment removed only 4 out of 67 ascarids and had no effect on the hookworms and whipworms present. It should be stated in comment that the areca nut used was ground 14 months previous to the experiment and hence may have lost some of its potency. This leaves open the question as to the efficacy of freshly ground areca nut, but it appears from the experiment that areca nut ground one year previously is not a very efficacious anthelmintic for dogs, and may possibly cause serious digestive disturbances. While it is not possible to determine whether the colitis noted in the dead dog resulted from the drug, it should be stated that this puppy had been weak and emaciated for some time previously and was in poor condition to undergo anthelmintic treatment.

FOR WORMS IN POULTRY.—Areca nut is quite commonly prescribed as a remedy for tapeworms in poultry. The following experiment was made to test its efficacy against tapeworms and incidental nematode parasites of the intestinal tract of chickens:

One gm. of powdered areca nut was given to each of six chickens, weighing about 453 gm. each, the dose being given in 4 mils of olive oil. Prior to the experiment the birds were fasted for 24 hours.

The total number of worms passed following the vermifuge were 20 *Heterakis papillosa*, which were passed by three of the six birds on the first day, and some tapeworm segments, including at least one head with these. On post-mortem examination large numbers of tapeworms and *H. papillosa* were found, besides other nematodes, which, from their location in the esophagus and proventriculus, would not be likely to be affected by anthelmintics. Probably more tapeworms were passed than were counted, since, when a small tapeworm head is passed and then given an opportunity to dry, it is very difficult to detect even by a careful examination of the feces. But at best the drug seems to have had very little efficacy against *H. papillosa* or tapeworms.

The areca nut used in this experiment was ground at least four years previously. This leaves open the question as to the efficacy of the freshly ground product. If it is true that the drug loses its potency after grinding, this constitutes a serious objection to its use in commercial products, since it is unlikely that it will be freshly ground when purchased.

SANTONIN

Santonin is the classic remedy for ascarids and forms the basis of most of the worm remedies for children. It has also been widely used and recommended in canine practice. As this drug is largely of Euro-

pean or Asiatic origin, the present price of santonin is almost prohibitive in veterinary medicine, and its place is being taken by the native and, in the writers' experience, more effective drug chenopodium. Santonin is usually combined with or followed by a purgative to promote elimination of the parasite. For this purpose calomel or areca nut is much used.

SANTONIN AND CALOMEL FOR WORMS IN DOGS.—The dose of santonin for dogs recommended by Winslow (*1913*) is from 1 to 3 grains (65 to 195 mgm.). Taking 130 mgm. as the dose for an average dog weighing 10 kgm., the writers gave seven dogs, ranging in weight from 3.8 to 9.5 kgm., doses graded from 32 to 130 mgm., accompanied by the same amount of calomel. The treatment was preceded by the administration of castor oil, 29.57 mils to dogs weighing 4.5 to 9.5 kgm., and 7.39 mils to pups under 4.5 kgm. Food was withheld the previous day. Seven ascarids (*Belascaris marginata*) were passed following the administration of castor oil and 13 *B. marginata* and two whipworms (*Trichuris depressiuscula*) after santonin and calomel. At the post-mortem examination it was found that about one-fourth of the ascarids remaining after the action of the castor oil later had been removed by santonin and calomel. The treatment was very inefficacious for whipworms, removing 2 out of 72, and entirely inefficacious for *Dipylidium caninum* and Taenia.

It would appear from the foregoing that santonin and calomel, the remedy usually prescribed for ascarids, is not very efficacious for dogs in single doses.

As the efficacy of the santonin as shown by the above experiment was considerably less than had been expected, considering the well-established reputation that santonin has as an ascaricide, a second experiment was undertaken to determine the efficacy of santonin and calomel in repeated doses. In this experiment four dogs, weighing from 1.8 to 9 kilos, were given graded doses of equal quantities of santonin and calomel, the dose varying from 32 to 130 mgm., according to weight. The first dose was given after a preliminary fast, and the second dose was given two days after the first, food being withheld the evening before the second treatment also, the same dose being given at each treatment. The first treatment was preceded by castor oil, which failed to eliminate any worms. One of the dogs passed no ascarids and had none post-mortem, so that it was evidently not infested and must be left out of consideration. From the three remaining dogs it eliminated 7 out of 10 ascarids, a distinct gain in efficacy compared with the previous experiment, in which a single dose was given. In this case the drug also showed a fair degree of efficacy against whipworms (*Trichuris depressiuscula*), parasites which in the writers' experience are difficult to remove with any degree of certainty with any of the anthelmintics tested. The drug was entirely ineffective against hookworms and *Dipylidium caninum*.

SANTONIN AND CALOMEL FOR WORMS IN HOGS.—Before the present European war, when the price of santonin justified its use for live stock, it was much recommended for roundworms (*Ascaris suum*) in swine. Since the separate dosing of a herd of swine requires considerable time and labor and the handling of the animals is likely to excite them and may lead to their being injured, it is usually the custom to mix the medicine with the feed, allowing a few hogs to eat from the same trough at one time. If the drug is well mixed with the feed and the animals are of about the same size, it is assumed that they will get approximately the same dose. This method was tested by the junior writer for a number of drugs. In this series of experiments the worms passed were not counted; nor were the animals killed. The feces were previously examined for ascarid eggs, and the efficacy of the drug was judged solely by the presence or absence of eggs in the feces three days after the administration of the anthelmintic, care being taken to verify all negative findings by one or more repeated fecal examinations at 3-day intervals.

In the first experiment, after a preliminary fast of 24 hours, three hogs weighing 15.4 to 18 kgm. were given santonin and calomel allowing 130 mgm. of each per hog. The drug was shaken up in 473 mils of water, poured over a bran-mash feed and thoroughly stirred in. The feces of all the pigs were positive for ascarids (*Ascaris suum* or *suilla*) at the beginning of the experiment. Three days after the treatment the feces of all the pigs were still positive. As the treatment failed to free any of the pigs from ascarids (*A. suum*), it was repeated, giving 194 mgm. of santonin and calomel instead of 130 mgm. The second treatment was equally without results. A third trial was made in which the pigs were dosed individually after preliminary starvation, each pig receiving 194 mgm. each of santonin and calomel. This treatment resulted in the apparent elimination of all ascarids from one of the pigs, the other two remaining infested. These hogs were then dosed individually with 259 mgm. each of santonin and calomel, all subsequent fecal examinations being negative.

It appears from the above that santonin and calomel should be given in repeated and separate doses to be effective. Probably three doses of santonin at intervals of three days would be effective. No symptoms of poisoning were observed either in dogs or pigs, although the pigs were given a dose more than twice as large as is usually prescribed for animals of their size. According to the Veterinary College at Ames, Iowa,[1] not over 4 grains (259 mgm.) of santonin should be given to the largest hog. It would seem that the treatment of swine with santonin requiring apparently three separate doses to be effective, is far too laborious and costly for use, especially as we have a more reliable and less expensive drug in oil of chenopodium.

[1] TREATING PIGS FOR WORMS. *In* Breeder's Gaz., v. 64, no. 8, p. 315. 1913.

SANTONIN AND ARECA NUT FOR WORMS IN DOGS.—Areca nut is frequently prescribed with santonin, since it furnishes the necessary laxative, and having anthelmintic properties of its own is supposed to be an adjuvant to the santonin. In this experiment four dogs weighing from 2.7 to 6.8 kgm. were given 33 to 130 mgm. of santonin combined with 0.78 to 1.94 gm. of areca nut. The dogs were given a preliminary dose of castor oil which removed 7 ascarids (*Belascaris marginata*). Following the administration of the santonin and areca nut 3 *B. marginata* were passed. At the post-mortem examination 30 ascarids (*B. marginata*) were found besides several hookworms (*Ancylostoma caninum*), whipworms (*Trichuris depressiuscula*), and 1 *Dipylidium caninum*. One of the dogs vomited the santonin, which may account for its failure to act in this case. In this case santonin proved less efficacious for ascarids than castor oil, and had no effect on the other intestinal worms present.

SANTONIN AND ARECA NUT FOR WORMS IN HOGS.—Combinations of santonin and areca nut are frequently prescribed for pigs, to be mixed with the feed. The following, copied from the Breeder's Gazette, is typical:

Santonin	2½ grains.
Areca nut	1 dram.
Calomel	½ grain.
Sodium bicarbonate	½ dram.

This quantity is considered sufficient for a 100-pound hog. As the pigs experimented with weighed only 24.5 kgm. each, two-thirds of the amount prescribed was allowed for each pig and mixed with the feed, after starving the animals 24 hours. Three days after the experiment the feces were still positive for *Ascaris suum*, and a second trial was made using the full amount prescribed in the formula. This experiment was also unsuccessful in ridding any of the hogs of ascarids. A third trial of the formula was made on a pig weighing 24.5 kgm. with the object of testing the efficacy of repeated doses. Five times the amount prescribed was made up and divided into seven powders, one powder being mixed with the feed every morning for seven consecutive days. At the end of the period no diminution in the number of ascarid eggs in the feces was discernible.

As far as these experiments can be analyzed, it appears that santonin and areca nut offer no advantages over santonin and calomel, and that either combination must be repeated and given in individual doses on an empty stomach to be efficacious. The last experiment illustrates the inadvisability of giving drugs to hogs, mixed with the feed, since in this case, a drug already shown to be efficacious in repeated doses was apparently a complete failure when given in this manner.

THYMOL.

FOR WORMS IN DOGS.—Prior to the beginning of the great European war, thymol was the classic remedy for hookworm in man, and it was only after the war had made this drug practically unobtainable that serious efforts were made to find a substitute for it. In a general way it was regarded as a satisfactory drug, and we expected to find a fairly high coefficient of efficacy for it in our experiments.

In our first experiment thymol was administered at the rate of 130 mgm. per kilo of body weight, giving the thymol in capsules to 2 dogs and in drench to 2 dogs; in the latter case the thymol was dissolved in a small amount of alcohol and this added to water to make a fine suspension. After an interval of a half hour to an hour, calomel in doses of about 65 mgm. per 2.5 kilos of weight of dog was given. All dogs were fasted from the previous day.

As regards hookworms, thymol removed 15 out of a total of 114 worms present, being entirely ineffective in the case of three dogs, two of which received the thymol in capsule and one of which received it in aqueous suspension. In one dog, however, it removed 15 out of 16 hookworms.

In regard to ascarids, thymol removed nearly three-fourths of these worms present, a very satisfactory showing considering that thymol is not usually considered especially valuable as an ascaricide. It was not efficacious when administered in aqueous suspension. Thymol also exhibited some efficacy against whipworms and was very slightly effective for *Dipylidium caninum*.

In the above experiment thymol showed a low degree of efficacy against hookworms, the parasite for which it is usually prescribed, and was more efficacious against whipworms and still more efficacious against ascarids. In the experience of the writers a number of drugs were found to be occasionally efficacious against whipworms, while at other times they were decidedly inefficacious. This variation may perhaps be explained as a matter of accident, depending on whether or not the drug succeeds in penetrating to the cecum in its passage through the alimentary tract.

An objection to thymol at present is its cost and scarcity.

In order to determine whether the low degree of efficacy displayed against hookworms by thymol was due to the mode of administration, the experiment was repeated. This time the animals were subjected to preliminary purgation with Epsom salt, and the administration of calomel after treatment was delayed for five to six hours. The thymol was given in the same dosage, 130 mgm. per kilo of body weight, and was given in aqueous suspension.

Three dogs weighing 4 to 9.3 kilos were used for the experiment. They were given Epsom salt at the rate of 3.7 mils for each 5 kilos of weight, the day prior to the administration of the anthelmintic, and five to six

hours after giving thymol they were given calomel at the rate of 65 mgm. for each 2.5 kilos of body weight.

One of the dogs died immediately after receiving the thymol, and the remaining two dogs each passed one ascarid. The post-mortem examination showed that one or both dogs were infested with hookworms (*Ancylostoma caninum*), whipworms (*Trichuris depyessiuscula*), ascarids (*Belascaris marginata*), and *Dipylidium caninum*. The treatment, therefore, proved an entire failure for all worms present except ascarids, for which it showed a rather low degree of efficacy in this experiment.

As the thymol used had not proved as efficacious against hookworms as might be expected, a sample was sent to the Biochemic Division of the Bureau for analysis. An analysis was made by Dr. Custis, who reported that it responded to all tests for thymol and showed no impurities. Thymol is apparently a stable phenol; the writers are unaware of any evidence indicating that it deteriorates.

Since thymol in a single dose proved so ineffective in the foregoing experiments, an experiment was undertaken to determine its efficacy in repeated doses. Four dogs weighing 2.3 to 3.9 kilos were given a preliminary purgation with 20 mils of castor oil on the day previous to treatment and were then fasted for 24 hours. Thymol was given at the rate of 130 mgm. per kilo of body weight, and this dose repeated three and five days later for a total of three doses. After the second and third doses of thymol, 97 to 130 mgm. of calomel were given. The first dose of thymol was given dissolved in alcohol to one dog and resulted in the immediate death of the animal. The other dogs were given the thymol in aqueous suspension.

The thymol removed 8 out of the 16 hookworms (*Ancylostoma caninum*) present in the dogs, a rather poor showing in view of the preliminary fasting, purgation, and repeated doses, but decidedly better than in the previous experiments. It removed the only ascarid (*Belascaris marginata*) present and showed some slight degree of efficacy against whipworms (*Trichuris depressiuscula*).

It appears from these three experiments that thymol to be at all successful as an anthelmintic for hookworms (*Ancylostoma caninum*) must be preceded by purgation and fasting and given in repeated doses. At least two such courses of treatment should be given to remove the greater number of the worms present, and further treatment combined with prophylaxis is desirable. As a matter of fact, this is the usual procedure in administering thymol in human practice, and it is usually realized by physicians that it is very difficult to remove all the hookworms present, as it is observed that hookworm eggs often persist in the feces after repeated thymol treatments.

In the three experiments considered together, thymol removed over half the ascarids present, but showed very little efficacy for whipworms or

Dipylidium caninum. That the administration of thymol to dogs is not without danger is shown by the death of 2 out of the 11 experiment animals.

The low efficacy and the danger in the use of thymol do not compare well with the comparatively high efficacy and safety in the use of chloroform, so far as the experiments with dogs are concerned. While the writers are impressed with the dangers in connection with the administration of most anthelmintics, and these dangers are quite impressive for chloroform as well as thymol, nevertheless, it seems that, with the exceptions already noted in the discussion of chloroform for cases where there is heart trouble, or lesions of the parenchymatous viscera, chloroform is not only much more effective than thymol, but, in therapeutic doses, is safer.

TURPENTINE

Turpentine is a remedy very commonly advocated for use against nematode parasites, especially those in chickens, horses, and swine. The obvious objection to its use is its well-known injurious effect on the kidneys.

FOR WORMS IN POULTRY.—Since the treatment of chickens for worms is for obvious reasons so seldom undertaken by veterinarians and so commonly by owners of poultry who are not especially trained in medical lines, it is not surprising that the dose advocated for use in this connection is very variable. Some writers recommend a half teaspoonful of turpentine in an equal amount of olive oil; others recommend 1 to 3 teaspoonfuls of turpentine undiluted.

An experimental test of the efficacy of the lighter dose of turpentine against worms in poultry was made as follows: Six chickens weighing between 0.45 and 0.9 kgm. were given 2 mils of turpentine mixed with 2 mils of olive oil, the birds being fasted from the previous day and the dose being followed at once with 8 mils of castor oil. About five hours after treatment all the birds had passed some feces, the feces having an odor of turpentine.

The treatment appeared to be fairly satisfactory for the large roundworm (*Ascaridia perspicillum*) in the small intestine of chickens, since it removed more than three-fourths of the worms present, as shown by post-morten examination. It had little effect in cases of infestation with large numbers of cecum worms (*Heterakis papillosa*) with which chicks are frequently infested. According to the experience of the writers, this worm is difficult to remove with any anthelmintic, since its location protects it to a greater or less extent from contact with the drug.

Turpentine was equally inefficacious as a remedy for tapeworms in fowls, removing only 8 out of 444. It should be stated, however, that it is very difficult to count the tapeworm heads which may be present in the

feces. On account of their minute size they dry quickly, and unless the feces are examined very soon after they are passed, many specimens will be unrecognized. The remedy, therefore, may have been more effective for tapeworms than the figures indicate. Its principal advantage, however, seems to be as a remedy for roundworms (*Ascaridia perspicillum*).

FOR WORMS IN DOGS.—Four dogs weighing 2.5 to 7.7 kilos were given preliminary purgation with castor oil, and dosed with turpentine at the rate of 1 mil per kilo of weight. The turpentine was given mixed with castor oil, 15 to 30 mils, according to the weight of the animals.

The preliminary purgation with castor oil did not bring away any worms. One of the dogs died on the fifth day after treatment.

Only one worm, an ascarid, was passed; to this should be added one ascarid found in the rectum of the dog that died, making two ascarids removed by the turpentine.

In view of the lack of results from the treatment, the dogs in this experiment were not killed. Just previous to the experiment, microscopic examination of the feces for eggs had shown that all of the dogs were infested with either hookworms or ascarids or both. On the last day of the experiment the feces were again examined for eggs, and eggs of the same worms were found to be still present.

All the dogs showed symptoms of distress immediately after the treatment with turpentine, the principal feature being a temporary paralysis of the hind quarters.

It may be concluded that turpentine in doses of 1 mil per kilo of weight is not very efficacious against ascarids in dogs, is entirely inefficacious against hookworms, gives rise to pronounced suffering and temporary paralysis of the hindquarters, and may kill the dog.

FOR WORMS IN HOGS.—Turpentine is frequently prescribed as a remedy for roundworms (*Ascaris suum*) in swine. It is often given in repeated doses mixed with the feed. A better way is to make an emulsion of the turpentine with equal parts of flaxseed decoction. This is more easily miscible with the feed, and avoids the burning caused by the ingestion of pure turpentine.

An emulsion of turpentine and flaxseed decoction, made by boiling 85 gm. of flaxseed in 296 mils (10 ounces) of water, straining, and adding an equal amount of turpentine, was fed to three hogs by the junior writer. The hogs weighed from 45.36 to 68.04 kgm. The equivalent of 7.4 mils of turpentine per hog or 44.36 mils of the mixture, was mixed daily in the feed of the three hogs for seven days. At the end of seven days all the hogs were listless, refused to eat, and were constantly voiding small amounts of urine, the nephritic symptoms continuing for a week after the treatment stopped. All the feces of the hogs contained ascarid (*Ascaris suum*) eggs after the experiment was concluded.

The treatment was decidedly inefficaceous and highly dangerous. The animals never gained as rapidly as the other hogs kept under the same conditions but not dosed with turpentine. While separate dosing might have shown some efficacy for the treatment, the injury to the hogs precludes its recommendation as an anthelmintic.

FICUS LAURIFOLIA

FOR WORMS IN DOGS.—The latex of *Ficus laurifolia* has been highly recommended by Berrio (*1911*) and by Mouat-Biggs (*1915*) for use in expelling whipworms from man, and is also said to have been adopted by the Venezuela State Board of Health as the official remedy for use against hookworms. Berrio gives doses of 25 to 30 gm., followed by castor oil. Mouat-Biggs gives the latex morning, noon, and night, mixed with water, which may be sweetened, or with milk, in doses of 10 to 40 gm., according to the age of the patient.

A sample of the expressed juice of the latex kindly supplied to the writers by Dr. Gonzalez-Rincones of Caracas, Venezuela, was tested on three dogs weighing from 4 to 29 kilos. Fifteen to 30 mils of the juice were given, preceded by a purge of 30 mils of castor oil, and followed three or four hours after the administration of the latex by 15 to 30 mils of castor oil. Although all the dogs were infested with hookworms, whipworms, or ascarids, as shown by a previous fecal examination, no parasites were passed. Since the remedy was entirely inefficacious, the dogs were not killed.

The sample forwarded to the writers did not conform to the published accounts of the latex, which describe it as of thick, sirupy consistency and milky white in color, but was instead a watery fluid with something resembling curds floating in it.

A second sample conforming in all respects to the descriptions of the latex was subsequently received through the courtesy of Dr. Rincones.

This drug was tested by the junior writer on three dogs weighing 4.5 to 18.2 kilos. The latex was given at the rate of 2.6 mils per kilo of weight and followed by castor oil at the rate of 3 mils per kilo of weight. The treatment was preceded by a dose of castor oil the day before, and the animals were starved for 24 hours. The drug removed 9 out of a total of 11 ascarids (*Belascaris marginata* and *Toxascaris limbata*), 1 out of 33 hookworms (*Ancylostoma caninum*), and 1 out of 50 whipworms (*Trichuris depressiuscula*), thus showing but little anthelmintic value for the two worms (hookworms and whipworms) for which it is particularly recommended, and a very satisfactory anthelmintic efficacy for ascarids. It was ineffective against *Dipylidium caninum*, no specimens being passed and several being found at autopsy. Of the three nematodes on which the latex had some effect, ascarids are, according to the experience of the writers, most easily removed—probably because they do not attach

themselves to the mucosa like hookworms and whipworms. The writers have usually found that any drug which is at all efficacious against hookworms is equally so against ascarids.

Evidently the latex has definite anthelmintic properties, and although its efficacy against hookworms (*Ancylostoma caninum*) and whipworms (*Trichuris depressiuscula*) was very slight in this test, it is worthy of further experimentation in repeated dosage. As the liquid expressed from the latex appears to have no value as a vermifuge, the active principle may be considered to reside in the solid portion sustained in the latex in the form of an emulsion.

SPIGELIA

FOR WORMS IN DOGS.—Spigelia, or pinkroot, is the dried rhizome and roots of *Spigelia marilandica*, a plant native to the Southern and Southwestern States. Its virtues as an anthelmintic are said to have been known to the Cherokee Indians. According to the U. S. Dispensatory, 19th edition,[1] it is generally considered among the most powerful anthelmintics, and is used especially for roundworms. The fluid extract is official.

A test of the fluid extract of Spigelia was made by the junior writer. In this experiment four dogs weighing from 4.8 to 18 kgm., all of which were infested with hookworms, and one with whipworms, were treated with Spigelia in doses graduated from 1.5 to 6 mils, according to the weight of the dogs. The drug was followed by 194 to 324 mgm. of calomel. The dogs were previously dosed with 29.57 mils of castor oil and then starved for 24 hours.

One dog was not killed, as it passed no worms. As the previous fecal examination for this dog showed hookworms, it is evident that the drug was ineffective in this case for hookworms. The three dogs remaining passed altogether 6 hookworms, including 3 found in the rectum postmortem in the process of elimination. There were 199 hookworms left unaffected by the treatment. Spigelia removed 1 out of 18 ascarids and 2 out of 29 whipworms. A few segments of *Dipylidium caninum* were passed, but no heads.

The remedy therefore appears to have but little efficacy as an anthelmintic for any of the common parasites of dogs, but further trial is advisable to determine this point.

TOBACCO

FOR WORMS IN CHICKENS.—Herms and Beach (*1916*) have devised a method of treating poultry for worms, consisting in the administration of chopped tobacco stems and the liquid in which they are steeped.

Finely chopped tobacco stems, 453 gm. or 1 pound, enough for 100 birds, are soaked for two hours in enough water to keep them covered.

[1] WOOD, G. B., and BACHE, Franklin. Op. cit., p. 1162.

Both the stems and water are mixed with half the usual ration of ground feed and given to the fowls. Two hours later one-fourth the usual ration is given mixed with Epsom salt at the rate of 312 gm. for each 100 fowls. The treatment is to be repeated one week later. The cost is said to be only 10 cents for 100 fowls.

In the present experiment six chickens were deprived of food for 24 hours and then fed the tobacco mash; two hours later they were fed the Epsom salt mash in the proportions recommended by Herms and Beach. The next day they were given what was left of the tobacco mash, since they had refused to clean it up the first time. A mixture of bran and tobacco was used, and the birds were not very eager for it, even after the preliminary fasting.

The remedy removed 30 out of 162 *Heterakis papillosa*, 3 out of 39 tapeworms, and had no effect on *Tetrameres* sp., a parasite which, from its location in the mucous glands of the proventriculus, would not be likely to be affected. This treatment is apparently intended especially for *Ascaridia perspicillum*, since the "roundworm" figured in the paper by Herms and Beach (*1916*) is evidently of this species. Unfortunately the efficacy of the treatment for this parasite could not be determined, since no species of Ascaridia were present in the birds used in the experiment.

While the tobacco treatment failed to free any bird from all of the worms of any given species that might be present, nevertheless the treatment seems to have been more successful against *Heterakis papillosa* or against tapeworms than the other treatments tried.

In view of the difficulty of removing *H. papillosa* from the ceca, it may be assumed on the showing here that this treatment would be effective in removing *Ascaridia perspicillum* from the small intestine, especially if the dose is repeated, as recommended by Herms and Beach.

OIL OF CHENOPODIUM

Oil of chenopodium is derived from the distillation of the seeds or of the entire leafy part of *Chenopodium anthelminticum* L., sometimes referred to under the synonym "*Chenopodium ambrosioides anthelminticum* A. Gray," and commonly called "chenopodium," "American wormseed," or "Jerusalem oak." According to Henkel (*1913*)—

> Wormseed has been naturalized in this country from tropical America and occurs in waste places from New England to Florida and westward to California.

Infusions made from chenopodium were used in the United States by the early settlers as a treatment for infestation with ascarids in man, and its anthelmintic properties are said to have been known by the Indians. Oil of chenopodium has only recently come into prominence as a result of the shortage of thymol and santonin, for which it has proved an effective substitute.

The chemistry of the oil of chenopodium has been studied by Nelson (*1911, 1913*), who was unable to ascertain its exact chemical nature, but concludes that it is an unstable dioxid. Its physiological action and toxicity have been the object of numerous experiments by Salant et al. (*1915*) and Nelson (*1911, 1913*). They note that it is a respiratory depressant and that it decreases vagus instability and diminishes frequency of heart action.

In regard to its toxicity the minimum lethal dose is twice as great when given by the mouth as when given hypodermatically. Repeated doses have a cumulative effect, and the toxicity is enhanced when the experiment animals are starved. It is less toxic when combined with nonessential oils, such as olive, cottonseed, or coconut oil. In cats 0.6 mil per kilo by mouth was invariably fatal, but in dogs 0.5 mil caused only vomiting. Adrenalin and digitalis were found to be antagonistic to oil of chenopodium.

Heiser (*1915*) notes that over 100,000 cases of hookworm infestation involving both *Ancylostoma duodenale* and *Necator americanus* have been treated in the Orient with chenopodium.

For worms in dogs.—In view of the present great interest in chenopodium, the writers have made a considerable number of tests of this substance with a view to determining its efficacy against worms in dogs and other domestic animals, and in nearly all cases they have found it extremely efficacious, especially for ascarids. The following experiment was conducted to determine the efficacy of oil of chenopodium when administered in one dose at the rate of 0.3 mil per kilo.

Eight dogs, weighing from 2 to 10.3 kilos, were given a preliminary purge of castor oil, which resulted in the removal of 9 ascarids. After starving for 24 hours, they were given chenopodium in the dosage indicated, mixed with 2.5 to 15.5 mils of castor oil, according to weight. The treatment was found extremely efficacious for ascarids, removing 160 worms and leaving only 2. From all but one of the dogs it removed all ascarids, and removed 10 out of 12 from that one. Its effect on hookworms and whipworms was less striking, about one-fourth of the total number present being removed. It had very little efficacy against *Dipylidium caninum*. It was evident that the dose given was unnecessarily large, since the feces smelled strongly of chenopodium, and six of the eight dogs vomited from two to four hours after treatment. An objectionable feature of the chenopodium treatment, as given, was the excessive ptyalism that it caused and the fact that the dogs objected to the taste of chenopodium in the castor oil and resisted its administration.

In the second experiment with chenopodium an attempt was made to overcome the ptyalism by giving the chenopodium in a capsule. Eight dogs, weighing from 5.5 to 9 kilos, were given chenopodium in capsules at the rate of 0.2 mil per kilo on each of three successive days, the drug being followed with five times its volume of olive oil the first two doses,

and five times its volume of castor oil the third dose. While this treatment removed 15 out of 17 ascarids (*Belascaris marginata*), it was ineffective for hookworms (*Ancylostoma caninum*), whipworms (*Trichuris depressiuscula*), and *Dipylidium caninum*. This method was less satisfactory than that employed in the previous experiment. The castor oil given was insufficient to overcome the constipating effect of the chenopodium; the chenopodium, being promptly released from the capsules, was brought undiluted against the gastric mucosa, causing considerable irritation, as shown by the fact that all dogs vomited promptly after the administration of the drug. Two of the dogs died from the treatment, one from traumatic pneumonia, due to the fact that the capsule opened in the larynx, allowing oil to penetrate the lungs. The other dog which died was a bitch, containing 11 well-developed fetuses, and it is likely that the pregnancy in this case was a condition contributing to the animal's inability to withstand the large amount of chenopodium given.

A third experiment was undertaken to test the efficacy of oil of chenopodium when given in doses of 0.1 mil per kilo, and the dose repeated daily for a total of six doses. The chenopodium was given mixed with 10 times its volume of olive oil, and was preceded each day by castor oil in amount equal to the olive oil; 1 minim of chloroform per kilo of weight was added to the mixture of chenopodium and olive oil the first day and to the castor oil on the following days. The animals were kept on half feed during the time the treatment was being given.

In this experiment all of the 8 ascarids present and 94 out of 133 hookworms were removed. This increased efficacy against hookworms is in the writers' opinion due largely to the chloroform administered with the chenopodium, since in none of their numerous experiments with chenopodium have they ever found it so efficacious for hookworms when given with castor oil only. The treatment was entirely ineffective for whipworms (*Trichuris depressiuscula*) or for *Dipylidium caninum*.

This method of administration proved generally satisfactory. The individual dose was sufficiently diluted to prevent any undue ptyalism when administered, and there were no symptoms of acute distress, which occurred when the oil was given in a capsule.

The results of this experiment led the writers to make another test of chenopodium and chloroform as a remedy for mixed infestation, chenopodium being in their experience the most successful remedy for ascarids and chloroform the best remedy for hookworms. This combination seems to be entirely compatible both physiologically and pharmaceutically. These drugs when combined with castor oil form a homogeneous and fairly stable mixture, and the action of each drug is not inhibited by the other.

Four dogs having been given a preliminary purgative of castor oil, followed by a 24-hour fast, were given chenopodium and chloroform, both

at the rate of 0.1 mil per kilo. The drugs were given in castor oil, varying in amount from 12 to 40 mils, according to the weight of the animals. In this case, as usual, the chenopodium proved efficacious against ascarids (*Belascaris marginata*), removing 7 out of 8. The remedy showed an appreciable effect on the whipworms (*Trichuris depressiuscula*), removing about one-fifth of the total number. In regard to hookworms, however, only 7 out of 61 were removed.

In order to ascertain whether the efficacy of the remedy for hookworms would be enhanced by increasing the dose, a second trial was made in which 0.2 mil per kilo, or double the amount of both chenopodium and chloroform, were administered. As in the previous case, the treatment was preceded by the administration of castor oil 24 hours before dosing, and the dogs allowed no food until after the administration of the anthelmintics. The chenopodium and chloroform were given in castor oil, allowing 29.57 mils for each dog. The preliminary purgative removed one ascarid (*B. marginata*) and some segments of *Dipylidium caninum*.

The combination of chenopodium and chloroform in the dosage given proved highly successful. All ascarids and over half the hookworms present were removed. As usual, it was entirely ineffective for *Dipylidium caninum*. Undoubtedly the dosage of chenopodium and chloroform at the rate of 0.1 mil per kilo is too small for the best results, and the efficacy of both drugs is enhanced by doubling the amount. At the same time this increased dose seems to be well within the limits of safety and has been tested several times by the junior writer, always with satisfactory results.

In view of the fact that castor oil is more or less objectionable to many persons and is not well tolerated by others, the writers undertook an experiment in which liquid petrolatum was substituted for castor oil in connection with oil of chenopodium. Four dogs weighing 4.5 to 15 kilos were given chenopodium in doses of 0.2 mil per kilo mixed with 10 mils of liquid petrolatum, the drug being followed at once by 20 mils of liquid petrolatum. The animals were fasted from noon of the previous day. One of the dogs died on the third day following the administration of chenopodium. The treatment was entirely inefficacious for ascarids, hookworms, *Dipylidium* sp., or *Taenia* sp., and removed only 2 of 28 whipworms. While the experiment indicates that the liquid petrolatum diminishes the efficacy of the chenopodium, it must be noted that there was only one ascarid present, and while the treatment should have removed the worm, this is a rather small basis on which to judge the performance of the anthelmintic. On the other hand, the liquid petrolatum seems to be unequal to the task of overcoming the constipation and toxic effects from the chenopodium, as the treatment resulted in the death of one dog.

It is the opinion of the writers that the mechanical lubrication resulting from the use of liquid petrolatum is not sufficient to overcome the constipation and that an active purgative, preferably castor oil, is indicated.

The foregoing experiments with chenopodium and chloroform, in comparison with other standard anthelmintics used for the removal of worms from dogs, indicate that oil of chenopodium is the best anthelmintic of those tried for use against ascarids (*Belascaris marginata* and *Toxascaris limbata*). In the 6 experiments, involving the use of 34 experiment animals, it removed 194 out of 200 ascarids, an efficacy of 97 per cent. It is at the same time probably a little more efficacious against whipworms (*Trichuris depressiuscula*) than any other anthelmintic tested. In the entire six experiments its average percentage of efficacy was only 12, a figure which illustrates the difficulty experienced in dislodging this parasite. Moreover, it is probable that the chloroform used in three of the experiments may be responsible for the removal of some of these worms, since both chloroform and chenopodium were found to have a limited efficacy for whipworms when given separately.

As regards hookworms (*Ancylostoma caninum*), the experiments of the writers with chenopodium do not show as high an average efficacy for this drug as they had been led to expect, considering the warm indorsement chenopodium has frequently received as an anthelmintic for the hookworm of man. Undoubtedly chenopodium as well as thymol would have to be given in repeated doses and the treatment renewed in order to secure a high percentage of efficacy. The writers have found chloroform much more efficacious than chenopodium for hookworms in dogs, and, when given at the rate of 0.2 mil per kilo, is apparently free from danger.

FOR WORMS IN HOGS.—A series of experiments to test oil of chenopodium as an anthelmintic for ascarids in swine were carried out by the junior writer and seemed to indicate the great value of this drug when given to hogs individually after a period of starvation. In these experiments the hogs were not killed, the effect of the anthelmintic being judged by the presence or absence of ascarid eggs in the feces passed subsequent to treatment.

In the first experiment with chenopodium an effort was made to determine the minimum effective dose necessary to free a hog from ascarids. In this case the dose of oil was combined with 3.7 mils of areca nut and mixed with the feed, after starving the pigs. Each pig was fed separately, thus assuring full dosage to each animal. Two pigs, weighing 11.32 and 14.06 kgm., respectively, were given 0.2 mil of chenopodium, while a third pig weighing 37.9 kgm. received 0.4 mil. This latter pig was apparently free from ascarids after a single dose, while the two other pigs each received three additional doses of 0.27 mil, 0.36 mil, and 0.54 mil before their feces were negative for ascarid eggs.

It is evident from the above that, even when given mixed with feed, a method later shown to be unsuitable, a relatively small dose of oil of chenopodium may prove efficacious. It should be stated in comment that at the time these experiments were conducted there was little

modern literature in regard to the use of oil of chenopodium, and, so far as the writer is aware, no use had been made of the oil as an anthelmintic for swine. Hence, the drug was administered cautiously. Subsequent experiments have shown that doses of chenopodium relatively many times larger are perfectly well tolerated by swine and are more certain in action.

In a second experiment with swine chenopodium was administered in castor oil, and was not given mixed with feed but was fed with a spoon to each hog individually. Four of the five hogs used were each given 28.35 gm. of Epsom salt mixed with their feed, while the fifth hog was given none. All animals were then starved for 24 hours before the administration of the chenopodium. The smallest pig, weighing 12.25 kgm. was given 0.8 mil; the others, weighing 12.7 to 28.12 kgm. were given 1 mil. The dose of chenopodium in each case was given with 29.57 mils of castor oil. This treatment was entirely successful. All five hogs had shown numbers of ascarid eggs in their feces prior to the treatment, and all were found free from ascarid eggs a week later. The feces of the hogs were again examined three days later and found negative. Two of the five hogs received a third fecal examination, which was consistently negative.

It appears from the above that chenopodium is an excellent anthelmintic when given in individual doses after preliminary starvation, and in most cases may be relied on to remove all the ascarid worms present. This opinion was confirmed by further experiments. The preliminary dosing with Epsom salt did not seem to be of any benefit, since the chenopodium was as successful in the case of the hog which received no salt as in the case of those that did. Subsequent experience has shown that in the chenopodium treatment for hogs preliminary purgation is an unnecessary expense.

As there is always a demand among stockmen for something that can be mixed with the feed to rid their hogs of worms, an experiment was undertaken to determine the possibilities of this form of medication. As hogs, especially if large, are very difficult to handle and as much time and effort would be required to dose separately each animal of a large herd, the advantage of mixing the medicine in the feed is obvious. Unfortunately this method proved impracticable, as shown by the following experiment.

One mil of chenopodium, 29.57 mils of castor oil, and 237 mils of linseed decoction made by boiling 113 gm. of linseed in 296 mils of water, were thoroughly shaken together into a homogeneous emulsion. This amount was allowed for each of four hogs weighing 20.4 to 32.2 kgm. The emulsion was distributed evenly through a bran mash which all four hogs ate together. The animals had previously been fed a mash containing Epsom salt at the rate of 28.35 gm. for each animal, then starved for 24 hours before treatment. The fecal examination a few days after

the treatment showed that one hog was freed from ascarids, the three others still remaining infested.

It is evident that the administration of drugs by mixing them with the feed is a method which gives little promise of success, and the far greater efficacy achieved when the drug is given individually after a fast more than compensates for the extra labor involved.

In order to be certain that the comparative failure in this treatment resulted from the method of administration and not from an insufficient dose of chenopodium, the experiment was repeated, allowing 2.5 mils of oil to each of the three hogs remaining infested. This experiment resulted in a total failure, all the hogs remaining infested after the experiment.

The above experiments were concerned solely with the action of chenopodium against ascarids, no attention being paid to its action on other intestinal parasites. In order to test its action on nodular worms (*Oesophagostomum dentatum*) three doses of oil of chenopodium were given to one hog at intervals of 10 days, two fecal examinations being made after each dose. The chenopodium was given with 3.7 mils of areca nut after preliminary starvation, and, so far as could be judged from the fecal examinations, there was no diminution in the number of nodular worms. On account of their location in the cecum and colon, where they are protected by a large mass of fecal material, it is not surprising that a vermifuge given by the mouth has little or no effect upon nodular worms. The extensive colon of the pig is rarely, if ever, approximately empty, even after prolonged starvation. Probably the best way to reach worms in this location is by the use of diluted anthelmintics in the form of enemata, as suggested by Railliet (*1915*).

As *Chenopodium anthelminticum* grows abundantly in the vicinity of Washington, D. C., a test was made to determine the possibilities of feeding the entire plants to the hogs. The test was made when the plants were in full seed and therefore contained the maximum amount of oil. A large armful of chenopodium plants was placed daily in a hogpen containing three hogs. The amount given represented about all the hogs would clean up in a day, and the experiment continued for 19 days. Although the hogs received their usual daily ration, they ate the chenopodium plants readily. At the end of 19 days one hog was apparently free from ascarids (*Ascaris suum*).

While this treatment has the obvious disadvantage of inaccuracy in dosage and is applicable only in those regions where the chenopodium plant grows abundantly, it has the great advantage of costing nothing but the labor of gathering the weeds. At least it would seem worthy of further trial.

A test of the dried seeds of chenopodium was made in the following experiment: Each of three infested hogs was given daily 3 gm. of chenopodium seed and 3 gm. of areca nut mixed with the feed. The

treatment was continued for 11 days, at which time each hog had received 33 gm. of chenopodium seed, or the equivalent of about 1 mil of the oil. One of the three hogs was apparently freed from ascarids.

The treatment, besides being of uncertain efficacy, cost more than a single treatment with chenopodium oil, since a large amount of both chenopodium seed and areca nut must be consumed. Its efficacy would doubtless be increased if given after a period of starvation, but this is obviously impossible when the treatment must be continued for several days.

It appears from the above experiments that oil of chenopodium is an excellent anthelmintic for ascarids in hogs when given in suitable dosage after a preliminary period of starvation. The best purgative with which to combine it is castor oil. This has the advantage of relative cheapness, certainty of its action, and of being easily miscible with oil of chenopodium. The chenopodium may be given first and followed immediately by castor oil, or the two may be given together. The efficacy of oil of chenopodium is greatly decreased or entirely lost if the drug is mixed with the feed and several animals allowed to dose themselves while eating together. Chenopodium seed and areca nut have but little efficacy when given daily, mixed with the feed, and the expense of this treatment, on account of the number of doses required, is actually greater than a single dose of the relatively high-priced oil of chenopodium. Chenopodium plants seem to have some value as an anthelmintic and, when these are available, the cost of anthelmintic treatment is greatly reduced. However, further experimentation is desirable along this line.

The following experiments with chenopodium, in which the hogs were subsequently killed and all worms counted, confirmed the writers' opinion regarding the efficacy of oil of chenopodium when given under suitable conditions:

Two pigs weighing 8.16 and 14.06 kgm., respectively, were given 1 mil of oil of chenopodium, while a third, weighing 9.98 kgm., was given 2 mils. The drug was followed by 59 mils of castor oil in the case of one pig and given in 59 mils of castor oil in the case of the second pig. Eleven ascarids and six nodular worms were passed by the pigs. Post-mortem examination showed that all animals were freed from ascarids (*Ascaris suum*), while numerous nodular worms (*Oesophagostomum dentatum*) were found in each animal. The experiment adds further proof of the efficacy of oil of chenopodium as an ascaricide, and demonstrates that it also has some efficacy for nodular worms, although probably only a few were removed. As already stated, these worms are so protected by the large amount of fecal material in which they lie that it is unlikely that any anthelmintic given by the mouth will have much effect upon them.

As already noted in the previous experiments, oil of chenopodium, when mixed with the feed of a number of hogs feeding together, had shown little or no efficacy as an anthelmintic. Since, however, in these

experiments the pigs were not killed and the results were based solely on the fecal examinations, it was decided to repeat the experiment, killing the pigs and counting the worms and thus determining definitely whether this method could be recommended.

A sow which had been starved for 24 hours was fed a mash of corn meal and bran into which had been stirred an emulsion consisting of 3.5 mils of oil of chenopodium, 60 mils of castor oil, and 473 mils (1 pint) of milk. Following the treatment the sow passed 19 stomach worms (*Arduenna strongylina*) and 13 nodular worms (*Oesophagostomum dentatum*). A post-mortem examination revealed the presence of 19 ascarids (*Ascaris suum*), 13 stomach worms (*A. strongylina*), and numerous nodular worms (*O. dentatum*). The treatment proved a complete failure in eliminating ascarids, thus confirming the opinion already expressed regarding the inefficacy of chenopodium when given mixed with the feed. The treatment removed over half the stomach worms present and demonstrates the possibilities of the drug for this species of parasite. Although it also had some efficacy against nodular worms, as usual the percentage removed was very small.

In cooperation with Dr. Ernest, of the Tuberculosis Eradication Division, of the Bureau of Animal Industry, the junior writer was recently enabled to make a practical test of the chenopodium treatment of swine on a large scale. The test was carried out at the Green Berry Point Farm of the United States Naval Academy, where about 176 swine ranging from young pigs weighing 15.88 kgm. or less to large boars and brood sows, were given the treatment.

The pigs were starved for 24 hours before treatment and confined in relatively small pens so that they could be easily caught. The brood sows and boars were kept separate. The pigs were caught in the small pen and lifted one at a time over the fence into a larger inclosure, where they were treated. Four laborers were employed in this work, two capturing the pigs and two holding the animals while they were dosed. Restraint was made fairly easy by backing the pig into a corner of the inclosure. While one attendant held the pig in this position the other kept the animal's jaws apart, using two loops made of harness straps; one loop, passing under the upper jaw, was pulled upward while the other loop, passing over the under jaw, was pulled downward. The head was kept tilted upward and the pressure on the straps, besides keeping the mouth wide open, served to hold down the tongue and prevent the hog from shaking its head.

A table to hold the bottles of chenopodium and castor oil and the measuring glasses was placed conveniently near. Four mils of oil of chenopodium and 1 ounce (29.57 mils) of castor oil was allowed each hog under 100 pounds (45.36 kgm.), while those over that weight were given double the dose. No attempt was made to weigh the animals, but the dose for each hog was decided upon as it was brought up for treatment. The

two oils were measured separately, and were then poured together into a large iron kitchen spoon, which was placed as far back as possible in the animal's mouth. Subsequently, however, the iron spoon was dispensed with, the oils being poured directly into the hog's mouth, care being taken to hold the graduate glasses out of reach of the hog's teeth.

When the medicine had been given the pressure on the straps was relaxed to enable the hog to swallow, the head still being held high. If the hog refused to swallow, it could always be induced to do so by plugging the nostrils with the finger tips. This forces the animal to breath through its mouth, and to do so it must first swallow.

We found this method fairly rapid for hogs weighing not over 100 pounds (45.36 kgm.), 65 animals being dosed in one hour. It took eight hours to dose the entire herd of 176 hogs, the labor of handling the heavy brood sows making the operation much slower than when pigs of medium size were being treated. In treating the brood sows it was necessary to throw them on their backs and to hold them in this position while dosing. As this caused considerable excitement to the sows, those which from their appearance were soon to farrow were left untreated.

Only one of the 176 hogs treated was injured. This animal, which was accidentally dropped, injuring the spinal cord, was killed and examined for worms. One hundred ascarids (*Ascaris suum*) were taken from a piece of intestine not over 30 cm. long, and many more remained uncounted. Two days later the manager of the farm reported that a great many ascarids were seen among the feces on the place, and about two weeks later one of the pigs which was killed for food was found to be entirely free from ascarids. The treatment therefore appears to have been very successful. The treatment required 1.13 kgm. of oil of chenopodium and 7.5 liters of castor oil. With chenopodium at $11 per kilo ($5 a pound) and castor oil at 66 cents per liter, the treatment in this instance cost a trifle under 10 cents per hog, exclusive of the labor. Even at the present high price of drugs, the cost is trifling compared with the increased profit which may be expected to be derived from healthy animals.

FOR WORMS IN SHEEP.—Four lambs weighing 16.6 to 26.1 kilos were dosed with oil of chenopodium at the rate of 0.2 mil per kilo, the dose which was found most effective for dogs. The medicine was given as a drench emulsified with 147.9 mils of milk. Following the treatment, one of the lambs contracted pneumonia, probably as the result of some of the drench's entering the lungs. The treatment succeeded in removing all the stomach worms from three lightly infested lambs, but failed completely in the case of one heavily infested lamb, suggesting that in this case the drench did not reach the fourth stomach directly, but was modified or absorbed in the rumen.

The treatment was fairly efficacious for hookworms (*Bunostomum trigonocephalum*), removing two-thirds of those present, in this respect

being considerably more efficacious than it was found to be against hookworms in dogs. It was inefficacious for other intestinal worms. On the whole, the use of chenopodium for stomach worms and hookworms in sheep seems to promise considerable success when properly administered, and is at least worthy of further trial.

FOR WORMS IN POULTRY.—To test the efficacy of oil of chenopodium against worms in poultry, six chickens were dosed at a rate of about 0.4 mil per kilo. Each bird weighed 0.5 kgm. Each bird received 2 mils of castor oil followed at once by 0.2 mil of oil of chenopodium mixed with 2 mils of castor oil, the birds being kept without feed the previous day. The treatment was fairly satisfactory for *Ascaridia perspicillum*, removing 9 out of 13 worms. In this connection it will be recalled that the experiment in feeding tobacco stems to chickens was carried out with birds not infested with *A. perspicillum*, so that the writers have no data of their own to compare with the showing made by oil of chenopodium. As already stated, Herms and Beach (*1916*) found the treatment very efficacious for worms which were evidently *Ascaridia perspicillum*, to judge from their illustration of the parasites.

Chenopodium removed only 2 out of 349 cecum worms (*Heterakis papillosa*) and was entirely inefficacious against other nematodes. No tapeworms were passed in the feces, but 22 were found post-mortem, 2 of which were in the large intestine. Even though these 2 are considered as having been removed by the anthelmintic, the showing is not very creditable. It may be stated, however, that none of the substances tested by the writers for tapeworms on poultry have proved very satisfactory.

DISCUSSION OF RESULTS

In order to present the foregoing data in a condensed comprehensive summary, the various experiments have been tabulated by hosts (Tables I–V). These tables show, for each host, the efficacy of the different drugs tested against the more important parasites, as indicated by the percentage of worms removed compared with the total number present. Three columns of figures are given for each parasite, in order that the reader may see at a glance not only the percentage of efficacy but the data from which this percentage is derived, and thus be able to judge how conclusive or otherwise the figures presented may be. The tables also show the number of host animals used for each drug tested, and the size of the dose, usually based on the weight of the animal. A reference column gives the pagination of the experiments described in detail in the text. Where several experiments have been conducted in testing one drug, the results are combined in the tables into a single set of figures.

While it is realized that in most instances these data are insufficient to express results in percentages, and for this reason reference to the percentage of efficacy of a drug has been avoided in the text, it was thought that comprehensive tables like the following would prove convenient in summarizing the results and would at least serve to indicate what drugs offer promise of success. Too much emphasis, however, should not be placed on negative results based in most cases on insufficient data.

The tables do not include some of the earlier experiments carried out on hogs, in which the efficacy of the drug tested was determined solely by the results of fecal examination without killing and examining the animals post-mortem.

TABLE I.—*Percentage of efficacy of various anthelmintics for dogs*

Drug tested.	Reference to experiment.	Number of animals treated.	Dose.[a]	Ascarids.			Hookworms.			Whipworms.			Dipylidium.			Taenia.		
				Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.
	Page.																	
Calomel and castor oil	399	4	260 to 324 mgm.	19	1	5												
Calomel (summary of several experiments).	.....	5	194 to 324 mgm.	33	0	0	5	1	20	3	0	0	6	(b)	0			
Epsom salt	400	3	4 gm. per 5 kilos	7	0	0	21	0	0	331	0	0	40	0	0	1	0	0
Castor oil (summary of 11 experiments).	399	50	3 to 40 mils	351	27	8	1,062	1	0.09	464	2	0.4	203	(b)	.....	3	0	0
Chloroform and castor oil	403	5	0.2 mil per kilo	4	1	25	830	474	57	48	7	15	255	0	0	.....	.....	.....
Iodoform [c]	405	4	0.2 gm.	(d)	.....	.....	(d)	.....	.....	(d)	.....	.....	(d)	.....	.....	(d)	.....	.....
Ether with castor oil	405	4	0.8 mil per kilo	23	8	35	503	0	0	.....	.....	.....	.....	.....	.....	1	(b)	100
Copper sulphate [e]	408	4	0.5 gm.	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Coal-tar phenols	414	2	0.48 mil	5+	2	40	3	0	0	.....	.....	.....	.....	.....	.....	(f)	0	0
Oleoresin of aspidium (summary of 2 experiments).	414	6	1 to 3 mils	33	5	15	18	1	6	16	0	0	6	4	67	4	4	100
Areca nut and soluble cream of tartar.	418	3	2 gm. areca nut and 12 gm. cream of tartar.	67	4	6	0	0	0	0	0	0	.....	.....	.....	.....	.....	.....
Santonin [g] (summary of 3 experiments).	420	15	16 to 130 mgm.	96	23	24	35	0	0	87	6	7	5	0	0	2	0	0
Thymol and calomel [h] (summary of 3 experiments).	423	9	298 to 1,752 mgm.	18	10	56	151	23	15	419	13	3	77	2	3	1	0	0
Turpentine and castor oil	426	4	2.5 to 7.7 mils	(i)	2	(j)	(f)	0	(k)	.....	.....	(k)	.....	.....	.....	.....	.....	.....
Ficus laurifolia [l] and castor oil	427	3	11.7 to 47.3 mils	11	9	82	33	1	3	50	1	2	18	0	0	.....	.....	.....
Spigelia and calomel	428	3	1.5 to 6 mils	18	1	6	205	6	3	29	2	7	1	(b)	0	.....	.....	.....
Chenopodium and castor oil (summary of 6 experiments).	430	34	0.1 to 0.3 mil per kilo	200	194	97	370	119	32	398	46	12	1,794	1	0.05	2	0	0
Pelletierine tannate and castor oil.	417	3	305 to 363 mgm.	3	0	0	9	0	0	5	0	0	1	0	0	(f)	(b)	100(?)

[a] The dose indicated is for the anthelmintic, not for the laxative with which it is combined.
[b] Segments.
[c] No parasites passed. Only two dogs killed, which were found infested with ascarids, whipworms, Taenia, and hookworms. Treatment proved entirely inefficacious.
[d] Present post-mortem.
[e] Prompt emesis; no anthelmintic action.
[f] Present, as determined by a microscopic examination of the feces.
[g] Showed 70 per cent efficacy when given in repeated doses and 100 per cent in individual cases.
[h] Showed 100 per cent efficacy against ascarids and 50 per cent against hookworms, in repeated doses.
[i] Unknown.
[j] Low efficacy for ascarids.
[k] Ineffective for hookworms and whipworms.
[l] Experiments with the liquid expressed from the latex of *Ficus laurifolia* showed that this substance had apparently no anthelmintic value (see page 427).

TABLE II.—*Percentage of efficacy of various anthelmintics for swine*

Drug tested.	Reference to experiment.	Number of animals treated.	Dose.[a]	Ascarids.			Whipworms.			Nodular worms.			Stomach worms.		
				Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.
	Page.														
Epsom salt in solution [b]	400	2	75.6 to 227 gm. in water.	....	....	....	....	....	....	....	....	....	....	....	....
Tartar emetic and castor oil.	401	2	360 mgm. in water.	29	5	17	9+	6	....	786	26	3	....	....	....
Chenopodium and castor oil.	436	3	1 to 2 mils.....	11	11	100	(c)	0	0	(d)	6	....	1	0	0
Emulsion of chenopodium and castor oil mixed in feed.	437	1	3.5 mils.....	19	0	0	0	0	0	(d)	13	....	32	19	59

[a] The dose indicated is for the anthelmintic, not for the laxative with which it is combined.
[b] Entirely ineffective. Pigs would not drink either the stronger or the weaker solution.
[c] Present.
[d] Numerous.

TABLE III.—*Percentage of efficacy of various anthelmintics for sheep*

Drug tested.	Reference to experiment.	Number of animals treated.	Dose.[a]	Stomach worms.			Hookworms.			Nodular worms.		
				Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.
	Page.											
Chloroform and castor oil.	404	[b]2	5 to 10 mils.....	14	9	64.0	5	0	0	6	1	17
Copper sulphate:												
In capsule.....	406	2	0.5 gm.....	10,541	41	0.3	.....	.....	.....	327	0	0
In drench.....	406	3	(50 mils of 1 per cent solution.)	726	674	93.0	.....	.....	.....	341	2	0.6
Gasoline in milk. (Summary of 3 experiments.)	409	9	7.5 to 30 mils.....	359	125	35.0	273	15	5	351	57	16.0
Petroleum benzin in milk.	411	2	15 mils.....	8	7	88.0	30	22	73	133	0	0
Coal-tar phenols in milk..	413	[c]6	2.8 to 15 mils.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Chenopodium.....	438	4	3.3 to 5.2 mils in 147.8 mils milk.	978	38	4	29	19	66	239	22	9

[a] The dose indicated is for the anthelmintic, not for the laxative with which it is combined.
[b] Both sheep died following the treatment.
[c] Two sheep died; the others passed no worms.

TABLE IV.—*Percentage of efficacy of various anthelmintics for poultry*

Drug tested.	Reference to experiment.	Number of animals treated.	Dose.[a]	*Ascaridia perspicillum.*			*Heterakis papillosa.*			Tapeworms.		
				Total number.	Number passed	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.
	Page.											
Areca nut with olive oil.....	419	6	1 gm.....	18	0	0	389	20	5	132+	1	....
Turpentine and castor oil.....	425	6	2 mils.....	66	50	76	463	10	2	444	8	2
Tobacco stems and Epsom salt..	428	6	454 gm. per 100 birds.	.....	.....	.....	162	30	19	42	3	7
Chenopodium and castor oil....	439	6	0.2 mil.....	13	9	69	349	2	0.6	22	2	9

[a] The dose indicated is for the anthelmintic, not for the laxative with which it is combined.

TABLE V.—*Percentage of efficacy of various anthelmintics for cats*

Drug tested.	Reference to experiment.	Number of animals treated.	Dose.[a]	Ascarids.			Taenia.			Hookworms.		
				Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.	Total number.	Number passed.	Percentage of efficacy.
	Page.											
Oleoresin of aspidium and calomel....	416	[b]6	0.8 mil.....	22	1	5	4	3	75	1	0	0
Pelletierine tannate and castor oil[c]..	417	2	64 mgm. per kilo.	....	....	....	....	....	....	....	....	....

[a] The dose indicated is for the anthelmintic, not for the laxative with which it is combined.
[b] Two cats died shortly after treatment. The third cat vomited one Taenia.
[c] Treatment was entirely ineffective. No tapeworms or nematodes removed.

CONCLUSIONS

Making due allowance for the paucity of data in regard to certain drugs, the writers consider that the following may be reasonably advanced as the result of their investigations.

Simple purgatives, calomel and castor oil, may have some slight value as anthelmintics, but it is hardly sufficient to justify their use for this purpose. Ascarids in dogs are sometimes removed by castor oil given as a preliminary purge, and this fact may prove of benefit in veterinary practice as a diagnostic measure when the more accurate method of microscopic fecal examination can not be carried out. However, castor oil failed to remove ascarids more frequently than it succeeded, and in no case were all the ascarids removed from any one animal. As many of the experiments on dogs were preceded by a dose of castor oil, the writers have fairly extensive data on this subject.

The most reliable vermifuge for ascarids, whether in dogs or swine, is oil of chenopodium. This drug, which was tested out on 34 dogs in six experiments, showed an efficacy for the entire series of 97 per cent. It rarely fails to remove all the ascarids present in a dog if given at the rate of 0.2 mil per kilo, preceded by a dose of castor oil and the animal starved for 24 hours before treatment.

The chenopodium treatment is also very efficacious for ascarids in swine, and when properly administered may be expected to remove most, if not all, of the worms present. It would seem, however, that neither chenopodium nor any other drug tested will give satisfactory results if mixed with the daily ration and the animals allowed to dose themselves; it is best given to each pig individually in suitable dosage, preceded by a fast. While this method necessarily involves considerable labor when treating animals as unruly as swine, the labor can be reduced by sorting the hogs roughly into classes according to size and confining them in inclosures which will permit them to be caught with a minimum amount of struggling. The treatment has proved practical on a large

scale and the results, as far as they could be determined, were entirely satisfactory.

Oil of chenopodium appeared to be effective for stomach worms in sheep, although the data on this subject are not sufficient to warrant its recommendation. It is also of some efficacy for hookworms in sheep and in dogs, though in the latter case chloroform was found more reliable.

Other remedies which seem to have more or less merit as anthelmintics against ascarids are the latex of *Ficus laurifolia*, santonin in repeated doses, and thymol. Although thymol in repeated doses is fairly efficacious against hookworms, it was inferior to chloroform for this purpose, causing more distress. An excellent preparation for mixed infestation in dogs consists of equal parts of oil of chenopodium and chloroform, given at the rate of 0.2 mil per kilo, combined with 30 mils of castor oil. This preparation may be expected to remove all the ascarids present, a large proportion of hookworms, and possibly a certain percentage of whipworms. This latter parasite seems to be very difficult to eliminate, and nothing tried by the writers proved very efficacious, almost any anthelmintic occasionally proving successful. This experience may perhaps be explained by an intermittent peristalsis of the cecum, which occasionally allows the anthelmintic to enter, but which usually excludes it. Although chloroform was fairly successful in removing stomach worms from sheep, both animals upon which it was tried subsequently died from its effects, and it would seem to be too dangerous for use on sheep.

In the case of stomach worms in sheep, copper sulphate was found to be the most satisfactory remedy, the experiments confirming the findings of Hutcheon. A simple apparatus (fig. 1) devised by the senior writer reduces the labor involved in drenching a flock of sheep and insures accurate dosage. Petroleum benzin also proved satisfactory and was more efficacious for hookworms than copper sulphate. However, it is much more expensive than copper-sulphate solution, must be given three times, and in a vehicle like milk, which adds greatly to the expense. The fact that petroleum benzin (refined gasoline) proved efficacious, while commercial gasoline was considerably less so, is perhaps related to the differences in specific gravity and consequent volatility of the refined product compared with the commercial product.

Among anthelmintics intended for use against tapeworms, male-fern proved efficacious when tested on dogs. In the case of cats it removed all tapeworms from 75 per cent of the animals tested, though it proved fatal to two out of six animals which were somewhat enfeebled from disease. Apparently it is more toxic to cats than dogs and should be prescribed with caution and only given to healthy subjects. So far as can be judged from a single experiment with dogs, there seems to be no danger in combining male-fern with castor oil, as is done in the so-called Hermann's mixture. In fact, the writers are inclined to agree with Seifert

(*1908*) that the administration of castor oil after male-fern will avoid the toxic effects of the latter by causing its rapid and thorough elimination, and that for this purpose no other purgative is quite so effective. This subject, however, should receive more study before conclusions are drawn.

Pelletierine tannate was a failure in the one experiment in which it was tested on cats, but was efficacious on dogs. No remedy was efficacious against tapeworms in poultry. Of the four drugs tested, chenopodium gave the best results for this purpose, but its efficacy for tapeworms is very slight.

Turpentine proved the most efficacious of the remedies tested on poultry for the removal of *Ascaridia perspicillum*, while chenopodium was nearly as good. When tested on dogs and pigs, turpentine was not very efficacious; and, as it caused grave symptoms of nephritis in pigs and caused the death of some of the experiment dogs, its use upon these animals is inadvisable.

The treatment with chopped tobacco stems recommended by Herms and Beach for ascarids in poultry proved fairly efficacious for *Heterakis papillosa* and would presumably be at least as efficacious for *Ascaridia perspicillum*, since this latter worm is more easily reached by anthelmintics than is *H. papillosa*.

There are a large number of drugs showing a greater or less degree of efficacy for the various intestinal parasites of domestic animals. Usually their action is selective—that is, they show a pronounced efficacy for certain species of intestinal worms, while they are decidedly less efficacious or entirely inefficacious against other intestinal parasites. If we consider the ideal anthelmintic one which will remove all worms of a given class or species, and do this every time in a single dose, we find that very few drugs approach this ideal.

Among the drugs which have given the best results under experimental conditions for the purposes intended and concerning which the writers have sufficient data to warrant positive conclusions may be mentioned the following:

(1) Copper sulphate in drench for stomach worms in sheep.
(2) Oil of chenopodium for ascarids in pigs and dogs.
(3) Oleoresin of male-fern for tapeworms in dogs.
(4) Turpentine for *Ascaridia perspicillum* in fowls.
(5) Chopped tobacco stems for *Heterakis papillosa* in fowls.

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TOBACCO WILDFIRE[1]

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INTRODUCTION

During the past season (1917) a leaf disease of tobacco (*Nicotiana tabacum*) has been the cause of much concern to tobacco growers because of its destructiveness. Attention was first directed to it during June when tobacco was being transplanted. Subsequently during the entire growing season numerous complaints of this disease were received by members of the staff of the North Carolina Agricultural Experiment Station and of the State Department of Agriculture. Because of the severity of the epidemic and the insistence by growers that this disease was manifestly different from any they had ever seen, an investigation was begun.

A preliminary survey of the literature on diseases of tobacco revealed the fact that this disease was clearly unlike any which had previously been described. Furthermore, the apparently water-soaked margin of the diseased areas, the tissues of which, upon microscopic examination, were found to be teeming with bacteria, suggested that the disease was probably of bacterial origin. Accordingly, attention in the first studies was centered upon the etiology of the disorder. A brief statement (7)[2] concerning this work, in which attention was directed to the presence of the disease, was duly prepared.

It was also pointed out that the causal organism was undescribed, and the name "*Bacterium tabacum* Wolf and Foster" was suggested. Promise was made in that report of a description of the morphological and cultural studies upon *Bact. tabacum*. Besides making this description, it is the present purpose to adequately describe the disease and to indicate our present knowledge of its economic importance, distribution, and dissemination.

HISTORY AND DISTRIBUTION OF THE DISEASE

While the disease was first definitely recognized in June, 1917, near Wendell, N. C., it is impossible to determine with certainty for how many seasons prior to the present one the disease has existed. It is quite probable, to judge from the testimony of several reliable informants, that the disease caused the loss of practically the entire crop in one field, near Wendell, in 1916. Mr. E. G. Moss, Assistant Director, in Charge of the Granville Branch Tobacco Station, Oxford, N. C., is convinced, as is also

[1] Approved for publication by B. W. Kilgore, Director, North Carolina Agricultural Experiment Station.
[2] Reference is made by number (italic) to "Literature cited," p. 458.

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the senior writer, that the malady was observed by him during 1916 at Creedmoor, N. C. To judge from the additional fact that the disease has been collected during the past season in 19 counties within North Carolina (Surry, Stokes, Forsythe, Guilford, Rockingham, Caswell, Alamance, Orange, Person, Durham, Chatham, Moore, Hoke, Wake, Johnston, Franklin, Granville, Vance, and Warren) and in 3 within Virginia (Pittsylvania, Halifax, and Mecklenburg) it is highly probable that the disease existed prior to the present year. Whether or not this disease occurs in other of the States in which tobacco is grown is not known, except in the case of Wisconsin. A letter from Prof. James Johnson, Department of Horticulture, University of Wisconsin, who has had occasion to observe the disease in North Carolina, states that a similar bacterial spot, although not nearly so destructive as in North Carolina, has been observed by him in Wisconsin.

ECONOMIC IMPORTANCE

The disease is universally conceded by growers of tobacco to be the most destructive one which attacks this crop. Losses, ranging from those which were inappreciable to those in which almost the entire crop was destroyed, were sustained in every locality where the disease was present. In some instances fields upon the same farm were observed to be badly affected, while others had little or none of the disease. In some sections, too, the disease occurred upon every farm within a radius of several miles, while in others it was present only in an occasional field. It is not possible, therefore, because the disease was not uniformly destructive over the entire area in which it is known to occur and because time has not been afforded to make a careful survey, to obtain a reasonable estimate of the damage wrought. Some idea of the losses, however, can be gained from statements taken from reports kindly furnished by a number of growers, who compared their leaf-tobacco sales with neighbors, whose crops were free from wildfire or were at most only slightly affected. Some of these reported losses averaging $100 per acre for their entire crop. One correspondent estimated his total loss at $5,000 and said that hundreds of farmers in his section suffered an equal acreage loss.

APPEARANCE OF THE DISEASE

The disease was first noted early in June during a period of rainy weather accompanied by nights which were so cold as to retard the growth of tobacco. The affected plants in many fields perished, necessitating replanting a second or a third time. A period of relatively dry, warm weather of about a month's duration followed, during which time, the crop made an extremely rapid growth, as shown by the fact that the plants were sufficiently mature to be topped. At this stage of their development another rainy season of about a week's duration occurred and was followed by another epidemic of the disease. The disease

appeared so quickly, spread so rapidly, and affected the leaves so seriously that it was commonly given the appropriate designation "wildfire."

The foliage alone seems to be subject to attack. The first evidence of disease is the appearance of circular, chlorotic areas varying from 0.5 to 1 cm. in diameter. Within 24 hours after this chlorosis is first noted minute brown areas will have formed at the centers of the spots (Pl. 15, A). Within another day these spots will have enlarged greatly Pl. 15, B), and a border of water-soaked appearance marks the margin of the necrotic tissues. Within a few more days the diseased areas are 2 to 3 cm. in diameter and are often strikingly concentric with shades of tan to dark brown, the centers being lightest in color (Pl. 16, A). Such spots have a broad translucent border, which is in turn surrounded by a chlorotic halo that pales out into adjacent tissues (Pl. 15, B; 16, A). When the spots are numerous, they fuse, causing large, irregular areas of leaf tissue to become dry. These dead areas remain intact in case there is no precipitation. When dewy nights and intermittent showers occur, however, the dead areas rot out so that the leaves present a ragged appearance (Pl. 16, C) which is especially manifest when large numbers of infections occur upon a single leaf.

Not uncommonly the leaves on one side of the plant are more seriously diseased than those on the opposite side and there may even be a unilateral destruction of these leaves resulting in distortion, as shown in Plate 16, B. The vascular tissues seem not to be invaded, but the organism confines its attack to parenchymatous tissues.

Two other leafspot diseases of tobacco, frogeye and speck, are present within North Carolina, from both of which wildfire is easily distinguishable. Frogeye appears as circular, brown spots, with a darker border and with grayish centers. Upon this gray center may be seen the fructifications of *Cercospora nicotianae* E. and E., or other fungi associated with the disease. No chlorosis accompanies these spots. Speck, which results from a deficiency of potash, appears as tan-colored, irregular areas which are first present at a distance from the principal veins. When this disease is accompanied by chlorosis, there is no definite halo around the lesions. In the case of neither of these diseases is the margin of the affected areas water-soaked in appearance, and in neither of them do the affected tissues disintegrate and fall out.

ISOLATIONS AND INOCULATIONS

On June 13, fresh material of tobacco wildfire was collected and isolations were made by planting on poured plates of nutrient agar fragments of tissue from the margin of affected areas. Contamination was avoided by washing the leaves prior to making the planting in mercuric chlorid and then rinsing them in sterile water. Several types of colonies developed along the margins of these plantings, the most common of which was *Bact. tabacum*, which appeared as glistening, grayish white

colonies. It was possible, in some cases, to make transfers directly from these colonies to tubes of agar and secure pure cultures. In others, dilution poured plates were first made, and the organism was transferred from certain of the colonies which developed to tubes of agar. Diseased material was collected several times subsequently, and numerous specimens were received by mail, so that opportunity was afforded during the season to isolate the organism from several sources.

Some preliminary inoculations were made on June 13 in which the inoculum consisted of macerated, diseased leaves upon which a quantity of water was poured. About 100 young tobacco plants growing in a flat in the greenhouse were then sprinkled with this water. Four days later infections were evident by the appearance of numerous yellow spots with pin-point-like centers.

On the evening of June 28 two potted tobacco plants, about 18 inches in height, were inoculated with pure cultures of *Bact. tabacum*. A watery suspension from agar cultures was sprinkled upon these plants, after which they remained covered with a bell jar for 36 hours. On the morning of July 2 numerous chlorotic areas had formed, which by July 5 had changed to large dry spots, typical of wildfire. No difficulty was experienced in reisolating the organism from these lesions.

On July 10, 16 plants which had been transplanted in the field on June 14 were inoculated by sprinkling them with suspensions made from bouillon cultures. These plants were not seen again until July 15, when large brown areas had formed abundantly, whereas adjacent uninoculated plants remained healthy.

Another series of inoculations, involving 18 plants growing in pots placed outside of the greenhouse, was made on July 25. In this case the leaves were immersed in a bacterial suspension. Seventy-two hours later the first evidence of infection was observed. Here again the organism was recovered from mature lesions.

Another set of inoculations, involving 12 potted tobacco plants, was made with what proved to be *Bact. tabacum* isolated from spots on cowpeas (*Vigna sinensis*) which had been planted between the hills in a badly diseased tobacco field. The spots on cowpeas, from which these isolations were made, were very similar in appearance to 3- or 4-day-old lesions on tobacco. Eight tobacco plants were inoculated on July 27 and four on August 2. Inoculation was effected by sprinkling the plants with a bacterial suspension. By August 1 in the first case and August 9 in the second there was no doubt that the diseased areas, which had formed upon all of the inoculated plants, were typical of wildfire. The organism was reisolated from these spots and, together with transfers from the original cultures from cowpeas, was used in inoculating cowpeas. Here again the same method as before was used in making inoculations. Only a few spots developed upon the several plants employed in two sets of inoculations. These spots were similar to those on cowpeas growing

in the field of diseased tobacco. Microscopic examination, furthermore, showed that the dead tissues were filled with bacterial organisms.

The lesions, both naturally and artificially produced, are believed to have originated around punctures made by leaf-hoppers, which were abundantly present on these plants throughout the season. The wildfire organism is capable of multiplying within the cells weakened as a result of the withdrawal of their contents by the feeding of these insects, but is not able to parasitize normal cells. Drops of moisture laden with bacteria certainly dripped from the diseased tobacco plants to the cowpeas beneath them, and could thus have supplied the inoculum which caused the cowpea foliage to become spotted. This explanation is supported by the observation that the lesions on cowpeas did not increase in size beyond pinpoint-like dead areas, indicating that *Bact. tabacum* can not adapt itself to invade healthy tissues, and by the further fact that no new spots developed subsequently on the naturally and artificially inoculated plants. Furthermore, spots never developed on cowpeas growing at a distance from diseased tobacco plants—that is, where they could not be infected through the agency of water dripping from diseased tobacco plants. *Bact. tabacum*, therefore, is not parasitic upon cowpeas, and its chance occurrence upon this crop indicates that conclusions as to the pathogenicity of bacteria when judged from inoculation experiments in which the inoculum is introduced through wounds are not entirely convincing. In view, therefore, of the fact that tobacco is not grown in the vicinity of West Raleigh, where the inoculation experiments were conducted, and that all of the uninoculated plants within the greenhouse grew to maturity without any manifestation of wildfire, there is no doubt that all of the infections which were secured resulted from inoculations with the organism in hand. When judged by the readiness with which infection occurs, *Bact. tabacum* is to be regarded as a very vigorous pathogene.

Aside from the inoculations upon cowpeas, only two other host species, bell peppers (*Capsicum annuum*) and Jimson weed (*Datura tatula*), were employed, with negative results.

PATHOLOGICAL ANATOMY

Affected tissues were fixed in 95 per cent alcohol, embedded in paraffin, sectioned, and stained with carbol-fuchsin. The presence of a crystalline substance whose nature is described in a recent paper by Ridgway (*3*) interfered seriously with the cutting of suitable sections. In tissues in which the cells had not yet become dry and collapsed, bacteria are abundantly present within the intercellular spaces (fig. 1). In mature lesions, however, they occur also within the cells. The contents of such cells appear to have been completely destroyed, whereas the walls have undergone little disintegration. The complete disintegration of diseased tissues, which occurs in the presence of excessive moisture, results, it

is believed, from the activity of other species of bacteria which enter the cells following invasion by *Bact. tabacum*. These species appear always to be present in old lesions as judged by the isolation studies.

DESCRIPTION OF BACTERIUM TABACUM

Bacterium tabacum, emend.

The primary cause of tobacco wildfire is a grayish white, rod-shaped organism with rounded ends. It is motile by means of a single polar

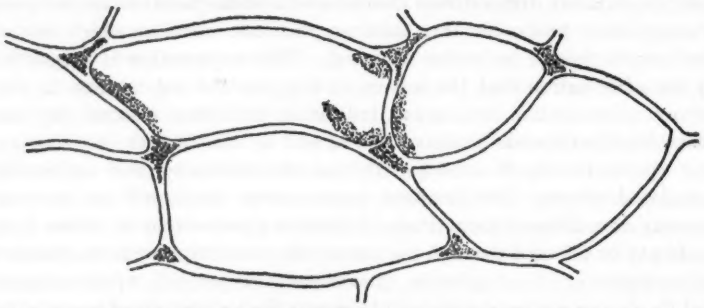

FIG. 1.—Parenchyma cells from the margin of a lesion showing *Bacterium tabacum* in the intercellular spaces and within the cells.

flagellum which is about twice as long as the body of the bacterium (fig. 2, *a*). Motility can be observed when fresh material is examined in a drop of water or when preparations are made from 18-hour-old bouillon or agar cultures. Flagella are easily demonstrated when the organism from such cultures is subjected to the staining method outlined by Morrey (*2*). The bacterium usually occurs singly within the host tissues, but in culture chains of as many as five elements have been noted (fig. 2, *b*). The limits of size vary from 2.4 to 5 by 0.9 to 1.5 μ, the most common size being 3.3 by 1.2 μ. No involution forms have been observed; neither have endospores been demonstrated.

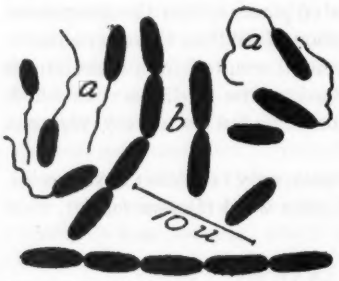

FIG. 2.—*a*, Flagella of *Bacterium tabacum* stained by Morrey's method; *b*, *Bact. tabacum* from bouillon stained with carbol-fuchsin, showing arrangement of the elements.

The organism stains readily with aqueous- and carbol-fuchsin, anilin gentian-violet, and methylene blue. It is Gram-negative, however, and is not acid-fast. Neither is a capsule demonstrable by the methods of Räbiger or Welch.

The organism has been cultured mainly upon glycerin agar and potato agar. Colonies appear in these media on the second day in poured plates

kept at a temperature of 20° to 25° C. By the fourth day the surface colonies have attained a diameter of 2 to 3 mm. They are grayish white in color, circular in outline, are appreciably raised, and have a smooth margin and a smooth, wet-shining surface. Buried colonies are biconvex.

In stroke cultures a filiform growth which widens at the base of the slant is formed. Growth is moderate and does not give rise to the production of odor. In stab cultures growth is best at the surface of the agar, and the line of puncture is filiform. In stab cultures on nutrient gelatin a filiform growth also appears along the line of puncture, with the greatest growth at the surface of the medium. No evidence of liquefaction occurs until the tenth day, when it becomes crateriform, and is complete within 30 days.

Growth on potato cylinders is nontypical in appearance, and there is no evidence of diastatic activity.

With a 2 per cent solution of Difco peptone as a basal solution, five solutions were prepared by adding 1 per cent of one of the following carbon compounds: Dextrose, saccharose, lactose, glycerin, and dextrin. No gas formed in fermentation tubes containing any of these media. A vigorous growth with strong clouding and a surface pellicle occurred in all in the open arm. In the presence of dextrose and saccharose a distinctly visible clouding gradually extended upward into the closed arm, while in the case of the other carbon compounds the closed arms remained clear. The organism is therefore regarded as aerobic in general.

Acid formation in stab cultures on litmus-glycerin, litmus-dextrose, litmus-lactose, and litmus-saccharose agar begins within four to six days, but no gas formation occurs on any of these media.

Growth on litmus milk presents a very characteristic appearance. During the first three days following inoculation there is a deepening of the blue color. Two days later coloration begins to become stratiform, and by the seventh or eighth day four distinct layers are evident. The upper one is between plumbeus and violaceous in color (*5*), the next is lilacinus, the third, violaceous, and the lowermost approximates cæsius. These colors lose their intensity after a few days and become more or less blended, and by the tenth day there is evident reduction of the litmus and precipitation of the casein. Reduction proceeds rather slowly and is complete by the twenty-fourth day.

There is no reduction of nitrates in nitrate-peptone broth, although a conspicuous clouding occurs. Furthermore, no gas is formed; and the tests for ammonia, indol, and skatol were negative.

The thermal death point of this organism, as determined by exposing newly inoculated tubes of bouillon in the customary manner, was found to be about 65° C. It is manifestly quite sensitive to desiccation, since no growth appeared after six days when bouillon cultures were placed on sterile slides in sterile petri dishes.

The group number of *Bacterium tabacum* according to the numerical system of the Society of American Bacteriologists is 2½1.2222032.

DISSEMINATION OF WILDFIRE

The fact that the disease appeared in epidemic form twice in one season and that each epidemic followed a rainy period, with little or no new infection in the interim suggests that dissemination is primarily influenced by moisture. This is in accord with observations on the dissemination of certain other plant diseases of bacterial origin, as angular leafspot of cotton (*4*) and Citrus canker (*6*).

Very striking evidence was found in two instances that wind is also a potent factor in the spread of wildfire. In one instance a field was observed before and several days following a rain which was accompanied by a high wind. The disease had advanced in consequence over a distance involving 16 to 18 rows lying parallel to diseased tobacco. The disease terminated rather abruptly beyond this distance. In another locality no disease occurred, except in the case of a field of approximately an acre in area, the plants for which had been brought for a distance of several miles. Here, again, the disease spread, following the same storm into an adjacent field to the leeward, was most abundant near the field of diseased plants, and gradually became less in the direction away from the diseased field. The organism had very evidently been spread by wind-blown rain, a phenomenon in accord with observations by Faulwetter (*1*) upon the angular leafspot of cotton.

When the first epidemic was prevalent in the vicinity of Oxford, N. C., thrips were abundantly present upon tobacco and were popularly suspected of being responsible for the spread of the disease. Accordingly, diseased leaves bearing numbers of these insects were collected, and the thrips were liberated upon healthy plants in the greenhouse at West Raleigh. Careful watch was kept, but no evidence of wildfire developed upon any of the plants. In the same season only a few thrips were found in diseased fields near Wendell, N. C., during an entire afternoon's search. For these reasons it is improbable that thrips are to be regarded as agents of dissemination.

Following the first outbreak of wildfire, opportunity was afforded to make numerous observations upon the origin of the disease. In every instance where the disease occurred in the field it has been possible to find that plants in the seed beds or "plant beds" were also affected. It was adjudged, therefore, that the disease must have been introduced into the plant beds either through the use of infected seed or through the agency of fertilizers. One large seed farm upon which diseased plants occurred was visited in searching for wildfire lesions upon seed pods, and, furthermore, affected pods were carefully sought for in many other diseased fields with negative results.

Since the disease is already so widely spread, which suggests that it must have had some common agency of dissemination, and since tobacco stems were incorporated in certain fertilizers as the source of potash, inquiry was directed to determine the possibility of the introduction and

dissemination of wildfire by fertilizer materials. Attempts to isolate *Bact. tabacum* from diseased leaves which had passed through the curing process gave negative results in the case of three samples tested. In view of the fact that no growth occurred in bouillon cultures exposed to temperatures above 65° C. for 10 minutes, as has previously been reported, it is highly improbable that the organism could survive for several hours temperatures of 180° F. and above, as are maintained for several hours in the last part of the curing process. Furthermore, in the preparation of tobacco stems for incorporation with fertilizer materials they are subjected to a sufficient degree of heat to insure complete sterilization.

SUMMARY

(1) A leafspot disease of tobacco called "wildfire," which is more destructive than any other malady affecting this crop, has appeared within North Carolina and Virginia.

(2) It has been collected during the past season in 19 counties within North Carolina, 3 within Virginia, and occurs also in Wisconsin.

(3) Wildfire first attracted attention at time of transplanting tobacco and appeared again in epidemic form at time of topping the crop.

(4) The disease originated in the seed bed or plant bed, but only negative evidence had been secured that infection comes from the seed.

(5) The leaves alone are attacked, and the symptoms are entirely unlike those of other foliage disease of tobacco.

(6) The primary cause of wildfire has been found to be a wet-shining grayish white, 1-flagellate organism, which is herein described as *Bacterium tabacum*. Its period of incubation is about 72 hours, and large lesions are formed within a week.

(7) The disease is of the necrotic type, involving parenchyma tissues.

(8) Moisture is of prime importance in the spread of wildfire. When rains are accompanied by wind, dissemination is especially rapid.

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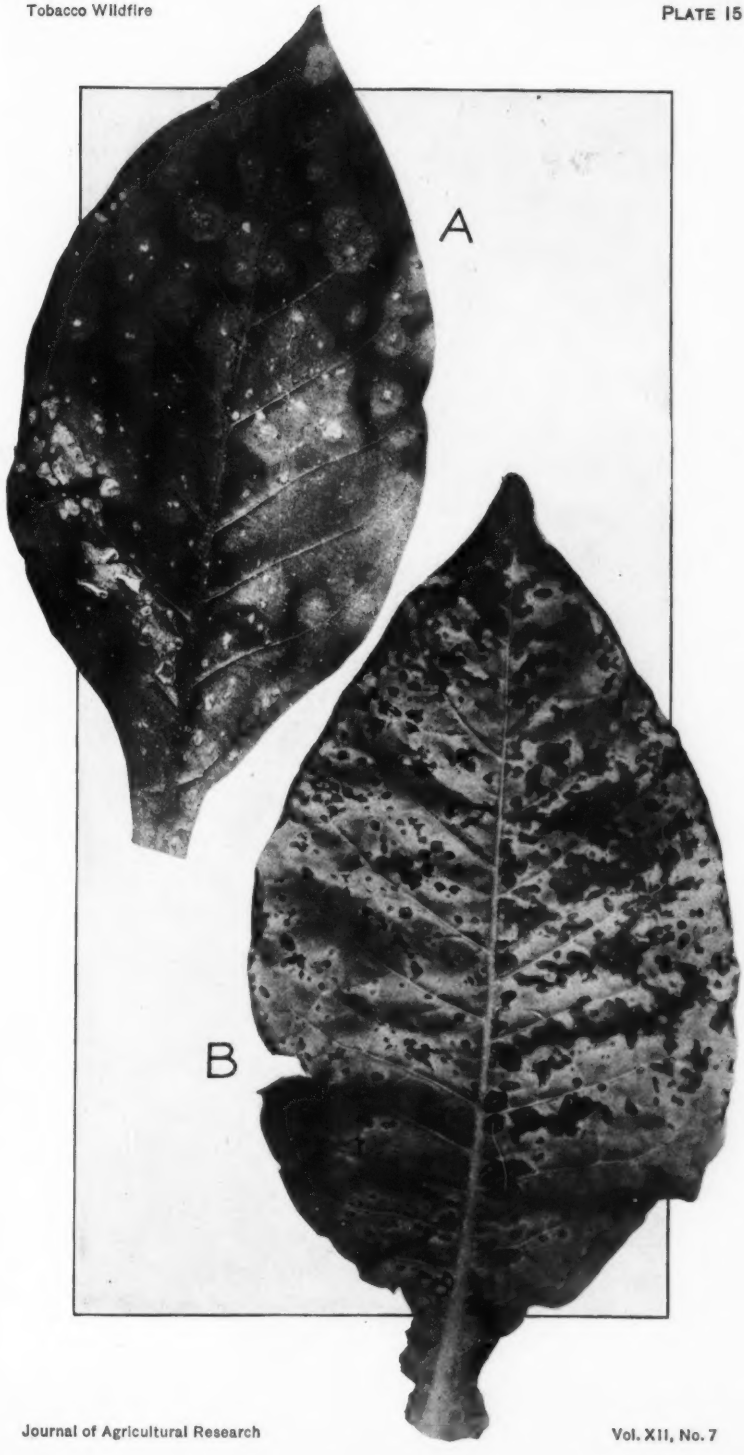
PLATE 15:

Bacterium tabacum:

A.—Tobacco leaf, four days after artificial inoculation, showing chlorosis and lesions.

B.—Natural infection with brown lesions bordered by tissues of a water-soaked appearance.


A
B

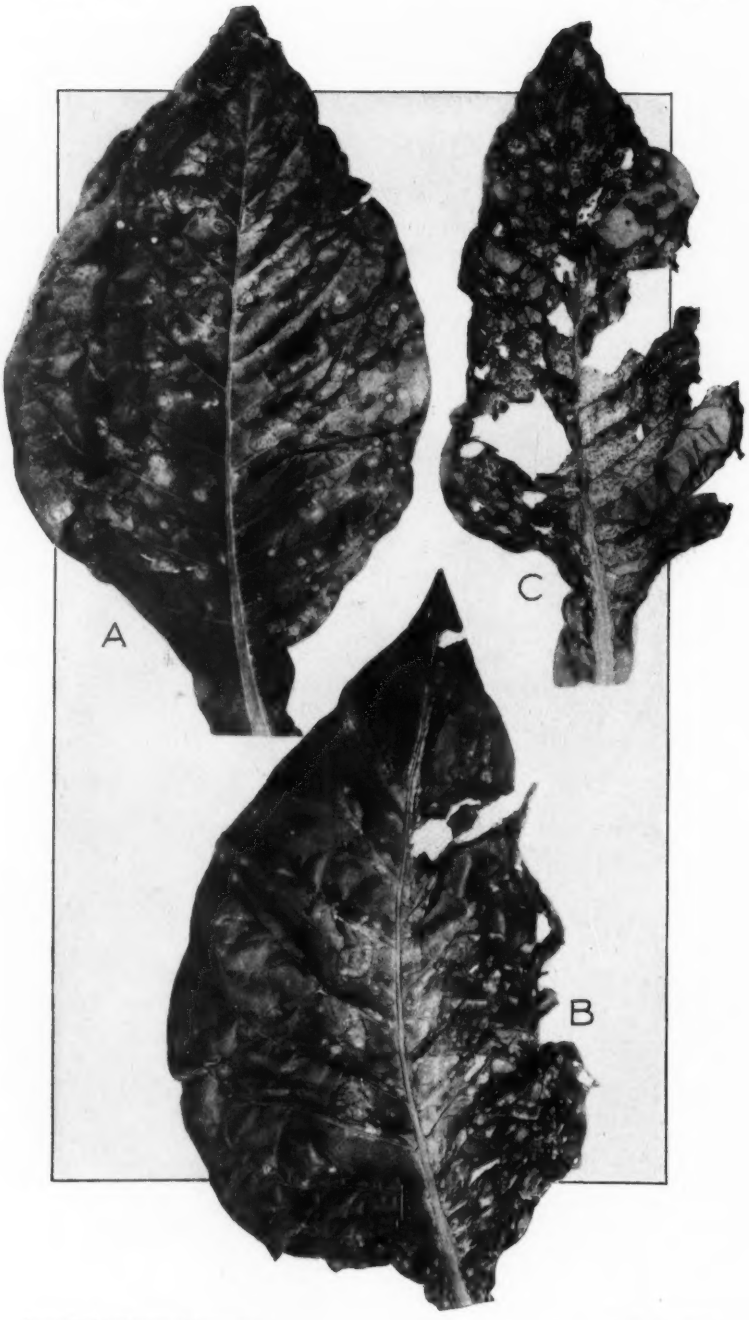

A
C
B

PLATE 16:

Bacterium tabacum:

A.—Natural infection. Lesions are large and concentrically zonate.

B.—Numerous confluent lesions on one side of the midrib have resulted in distortion of the leaf.

C.—Almost the entire leaf is involved and a portion of the rotted tissues have fallen out. Natural infection.

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GIPSY-MOTH LARVÆ AS AGENTS IN THE DISSEMINATION OF THE WHITE-PINE BLISTER-RUST[1]

By G. FLIPPO GRAVATT, *Assistant Pathologist*, and G. B. POSEY, *Scientific Assistant, Investigations in Forest Pathology, Bureau of Plant Industry, United States Department of Agriculture*

INTRODUCTION

Very little has been done to correlate the widespread distribution of the white-pine blister-rust, caused by *Cronartium ribicola* Fischer, with factors governing the dissemination of the spores of the causal organism. The early occurrence of telia on leaves of currant and gooseberry plants (*Ribes* spp.) in localities distant from known infections on pines (*Pinus* spp.), together with the absence of definite knowledge of instances of overwintering on the former hosts, is suggestive of distant seasonal spread of the disease by æciospores from pines.

Larvæ of the gipsy moth (*Porthetria dispar* L.) feed on the Peridermium stage of *Cronartium ribicola* and carry thousands of æciospores on their bodies. As Collins[2] found that larvæ of the gipsy moth are blown as far as 20 miles, these insects are a potential agent in distant spread of the blister-rust. The gipsy moth is distributed over a large portion of the white-pine region of New England.

GIPSY-MOTH INFESTATION ON DISEASED PINE

In the fall of 1916 a stand of white pine covering an area of from 5 to 7 acres at Kittery Point, Maine, was found to be severely infected with *Cronartium ribicola*. This growth ranged from young seedlings to mature trees 80 feet tall and random ¼-acre plots in this area showed 65 to 100 per cent of the trees to be diseased. The number of infections on individual trees ranged from 1 to more than 300, and it was estimated that there were 75,000 to 100,000 separate infections in trees on this area.

In the infected plot gipsy-moth-egg clusters were found in varying abundance on limbs and stems of pines of all sizes, and were located from near the ground to the tops of the largest trees. In a number of cases egg clusters were present on the diseased bark, and in one instance four were located on a single canker.

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[1] The writers are indebted to Mr. A. F. Burgess, of the Office of Gipsy Moth and Brown-tail Moth Investigations, Bureau of Entomology, for helpful suggestions. Further work is being carried on in cooperation with the above office.

[2] COLLINS, C. W. DISPERSION OF GIPSY MOTH LARVÆ BY THE WIND. U. S. Dept. Agr. Bul. 273, 23 p., 7 pl. 1915. Bibliography, p. 22–23.

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On May 25, 1917, large numbers of gipsy-moth larvæ were found in and around ruptured blisters, and several days later some of the blisters where the presence of larvæ had been previously noted were empty, and spore production was apparently arrested. Subsequent observation on these blisters showed that no further spore production took place, while on the same cankers blisters which were artificially protected from larvæ continued to produce spores in abundance until June 25. To determine the rate of blister destruction on June 9 a number of larvæ were placed on a twig infection which had 38 sporulating pustules. Many of the larvæ crawled away or dropped off, but a sufficient number remained to destroy the fruiting layer in practically every blister by noon of the following day, with the result that no subsequent spore production took place.

Cessation of spore production in injured blisters was caused by the destruction of fruiting hyphæ. Usually the spores and hyphæ were eaten away first and then the larvæ very often ate through the base of the fruiting layer to a depth of several millimeters. Apparently, after blisters no longer furnished suitable food for the larvæ, they began feeding on the areas of the yellowish, discolored, infected bark outside the fruiting region and in some cases a large per cent of the outer bark of next year's sporulating zone was destroyed. Careful observations on many larva-infested cankers showed that spore production was prematurely arrested in 25 to 100 per cent of the pustules, the percentage usually averaging highest on small twigs.

SPORES ON LARVÆ

Larvæ working in blisters collected so many æciospores on their hairy bodies that they appeared nearly the color of spores in mass. On different dates larvæ were taken from blisters and placed in separate capsules, precautions being taken against including spores not on the bodies. These were taken into the temporary laboratory and spore counts made of the bodies and the alimentary tracts. Spores for counting were removed from larvæ by washing the bodies in series of water, and alcohol mounts on slides followed by final examinations to assure thoroughness in the method used. This procedure proved quite effective, and, where carried through 5 to 10 washings, practically all spores were removed from the outside of the bodies. Counts were made on the spores adhering to the inside of the capsule and added to the total found in the washings. After bodies of the larvæ had been thoroughly washed, they were dissected and counts made of spores in the alimentary tracts. On May 26, June 4, and June 11 fifteen small larvæ were collected. Spore counts on the bodies of these 15 gave a minimum of 1,120, a maximum of 28,320, and an average of 18,100. Counts of spores in the alimentary tract gave a minimum of 1,740, a maximum of 48,570, and an average of 26,022

To determine the approximate amount of spore material passed through the alimentary tract, 20 larvæ were placed on fresh cankers in a feeding tray. After they were settled and had fed normally for several hours, a sheet of paper was placed under the cankers for the collection of pellets. A total of 423 pellets were dropped within a period of 13 hours. Counts of the spores in these pellets gave from 3,960 to 12,450, with an average of 8,160, which is at the rate of 318,616 spores excreted per day per larva.

Germination tests made of the spores on the bodies of larvæ collected on cankers gave positive results, and approximately the same percentage of germination was observed as on spores taken directly from these cankers. Germination tests of spores in pellets have given very poor results; in only one case did several spores germinate. In many cases spores taken directly from these cankers also failed to germinate in laboratory tests.

WIND DISPERSION OF LARVÆ AS A FACTOR IN BLISTER-RUST SPREAD

At Kittery Point, Me., æciospores were produced from April 29 to July 1, with maximum spore production from May 10 to 25. Collins[1] gives the hatching period for gipsy moth larvæ in this section for 1912, 1913, and 1914 as May 1 to 23, April 29 to May 14, and May 11 to 28, respectively. The season of 1917 was approximately one week later than usual. The period of wind dispersion of larvæ is given as ranging from 18 to 30 days, starting one to two weeks after the first caterpillars hatched. Observations by the writers showed varying numbers of larvæ feeding on blisters from May 25 to June 25.

Collins[2] working with wind dispersion of larvæ of the gipsy moth over a series of several years showed that they were carried in wind currents to distances as great as 20 miles. The same author states that approximately 50 per cent of the larvæ caught at distances of 6 miles or less had fed previously.

The writers, using fly-paper traps, placed 10 to 30 feet from the nearest pine infection, and so arranged as to exclude larvæ that may have reached the trap by crawling, caught 75 small larvæ. Four of these caterpillars had, respectively, 35, 105, 185, and 2,180 æciospores on their bodies, which establishes the fact of local wind dispersion of æciospore-bearing gipsy-moth larvæ. That spores carried on bodies of larvæ may remain viable for a considerable length of time is borne out in viability tests under laboratory conditions, wherein æciospores germinated after remaining in vials for a period of two months.

Examination of wild and cultivated species of Ribes at various points throughout Kittery Township showed an abundance of gipsy-moth larvæ feeding on the foliage, and in many cases they were observed crawling on the under surfaces of leaves. Quite a number of the larva-

[1] Collins, C. W. 1915. Op. cit. [2] Collins, C. W. 1917. Op. cit.

infested plants showed areas producing uredospores, and in four instances the only leaves showing blister-rust infections were those which had been injured by insects.

Sixty larvæ collected on species of Ribes were examined for æciospores. Of these one larva collected on June 14 on the under surface of a wild gooseberry plant showed 280 æciospores and 520 uredospores on its body. The gooseberry plant was heavily infected with blister-rust, being located only 20 feet from pine infections. Germination tests of the spores from this larva gave two germinating æciospores and many germinating uredospores, thus bearing out the fact that gipsy-moth larvæ do carry viable spores to *Ribes* spp. and also showing the part which insects may play in local distribution of the disease by uredospores.

PRACTICAL IMPORTANCE

The facts given in regard to the gipsy-moth larvæ show that these insects are certainly a factor in the spread of the blister-rust locally from pines to *Ribes* spp. Their habit of feeding and crawling over the lower leaf surface, where the stomata are located, gives the spores borne on their bodies a good opportunity for causing infection. The probability of the spread of blister-rust from pines to distant *Ribes* spp. is undoubted, since Collins' work shows that the gipsy-moth larvæ are blown by winds of varying intensity for distances of 20 miles. Though wind is considered to be the most important factor in æciospore dissemination, gipsy-moth larvæ undoubtedly play an important part. Other insects have been collected from infected pines with thousands of æciospores on their bodies, but these insects were not present in sufficient numbers to make them of importance in comparison with the number of gipsy-moth larvæ present.

SUMMARY

(1) The period of hatching and of wind dissemination of gipsy-moth larvæ came within the period of spore production of the blister-rust on pines.

(2) Larvæ fed abundantly on spores and injured the fruiting layer of the pustules so that further spore production was arrested.

(3) Larvæ from blister-rust cankers had thousands of viable spores on their bodies. A small percentage of the larvæ collected from fly paper and from species of Ribes near infected pines showed æciospores on their bodies.

(4) Gipsy-moth larvæ were found feeding on leaves of *Ribes* spp., and in some cases the only infected leaves on plants of this genus were those showing insect injury.

(5) The Bureau of Entomology has shown that these larvæ are blown by the wind up to a distance of 20 miles. Within this distance the larvæ are potential agents in the spread of the white-pine blister-rust (within the area infested by the gipsy moth).